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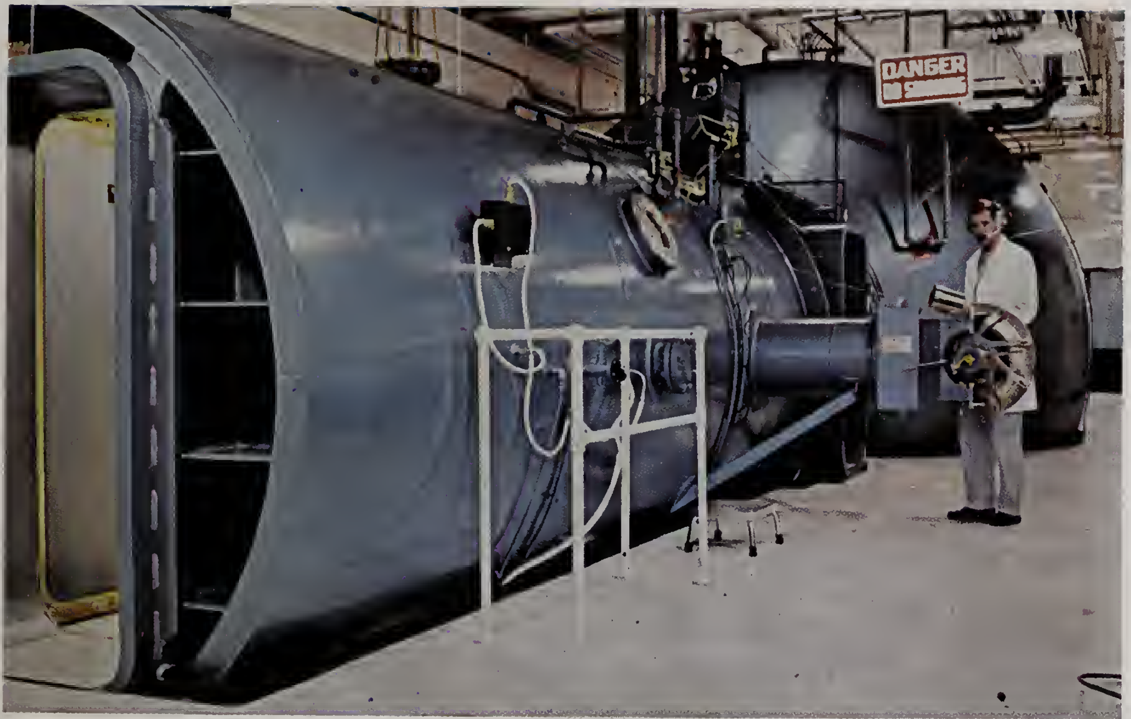

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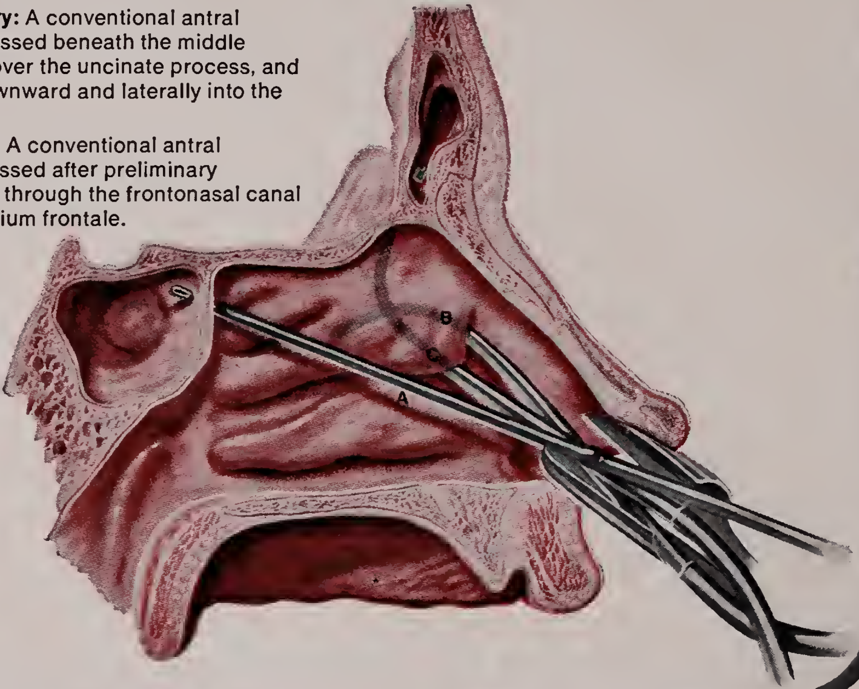

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*Reed, G. F.: Sinusitis, New England J. Med. 267:402, Aug. 23, 1962.

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1. Griffith, R. S., and Black, H. R.: Current Ther. Res., *6*:253, 1964.

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Pseudohypoparathyroidism

• Followup • Over • A • 26 • Year • Period

STEPHEN A. KIEFFER, M.D.*†
DONALD H. PETERSON, M.D.§
J. RICHARDS AURELIUS, M.D.*‡
St. Paul, Minnesota

PSEUDOHYPOPARATHYROIDISM was first described as a clinical syndrome by Albright and his group in 1942.[1] The sine qua non for its diagnosis is the presence of clinical and laboratory evidence of chronic parathyroid insufficiency without evidence of renal disease, steatorrhea, or generalized osteomalacia. As a corollary, prolonged daily injections of parathormone fail to produce the hypercalcemic response seen in individuals with idiopathic hypoparathyroidism.[2]

Surks and Levenson[3] have recently summarized the findings in 59 cases reported in the literature. All but three of these patients gave a history of convulsions or their tetanic equivalent. The typical habitus described by Albright** (short thick-set features with round facies) was found in 47 cases (79%). Twenty-nine cases (49%) showed ectopic calcifications in the subcutaneous tissues. Osseous dysplasia, chiefly involving the metacarpals and metatarsals, was noted in 31 patients (53%). Less frequent findings include calcification of the basal ganglia, lenticular opacities, mental retardation, and disturbed dentition.

Report of a Case

A 27-year-old Caucasian female was admitted to Ancker Hospital neuropsychiatric service in March, 1962, having recently been discharged from the care of the staff of the Mayo Clinic, who made the diagnosis of pseudohypoparathyroidism. She gave a history of lifelong obesity. At age 17 she left school, having reached only the ninth grade. For the previous three years, she had noted recurrent cramping and numbness in the extremities and an intolerance to cold.

Physical examination revealed a short (57 inches), fat (181 pounds) female, who answered questions haltingly. The face was round and the neck very short; the hands were chubby and the fingers short, with bilateral absence of the knuckle prominences for the fourth and fifth fingers. Trousseau's sign was positive, and Chvostek's sign was present. She had a normal female hair distribution.

Laboratory values included a serum calcium concentration of 6.9 mg. per cent (normal 9.0-11.0), serum phosphate of 5.2 mg. per cent (normal 3.0-4.5), and a 24-hour total urine calcium of 9.6 mg. (normal 50-300). Parathyroid hormone given intramuscularly in daily doses for two weeks failed to elicit a rise in the serum calcium. Her basic metabolic rate was minus 10 per cent, and a serum protein-bound iodine concentration was 3.8 micrograms per cent (normal 4.0-9.0). A 24-hour I^{131} uptake study showed a value of 12 per cent (normal 15-45). After TSH stimulation, however, this value rose to 37.5 per cent, establishing a diagnosis of secondary hypothyroidism. Radiographic findings will be described later. Her intelligence quotient (Wechsler full scale adult) was 63, placing her in the lowest one per cent of the adult population.

---

*From the Departments of Radiology, Ancker Hospital, Saint Paul, Minnesota, and University of Minnesota Hospitals, Minneapolis, Minnesota.

†Medical Fellow Specialist in Radiology, University of Minnesota Hospitals.

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‡Emeritus Chief, Department of Radiology, Ancker Hospital, Clinical Professor of Radiology, University of Minnesota Medical School.

**See page 13.

A psychiatric consult was as follows: "Mixed psychoneurosis with depressive anxiety and hysterical features in a passive, obese woman of low mentality who is understandably quite concerned about her appearance."

The patient was treated with calcium lactate, calcium gluconate, and vitamin D_2. Although her mental state did not improve, the serum calcium and phosphate values rapidly attained the normal range. When last seen in this clinic in September, 1963, the serum calcium and phosphate were 9.5 and 3.5 mg. per cent respectively.

Radiographic Findings

Cusmano, Baker, and Finby[4] have summarized the radiographic findings in pseudohypoparathyroidism. The most frequent finding in their series was shortening of the fourth and fifth metacarpals and less frequently the first metacarpal. The fourth and fifth metatarsals also were often shortened. Less frequent radiographic findings have included calcification of the basal ganglia, ectopic calcifications in the soft tissues in the vicinity of the joints of the hands and feet, and thickening of the bony calvarium. The latter finding involves a widening of the diploic space rather than actual cortical thickening of the inner or outer tables of the skull. These authors also noted accelerated skeletal maturation in four of their six patients.

The Metacarpals and the Metatarsals

Films of our patient on the most recent admission are shown in Figures 1, 2, and 3. Figure 1 shows marked bilateral shortening of the fifth metacarpals and to a lesser degree of the fourth metacarpals. The shafts of the fifth metacarpals are also widened.

Figure 2 shows bilateral shortening of the fourth metatarsals which are also widened in comparison with adjacent metatarsals. Figure 3 demonstrates the widening of the diploic space of the calvarium.

A review of the patient's chart and film jacket revealed that she had been seen at age 11 months because of delayed development. Films of the hands and feet, now over 26 years old, show accelerated skeletal maturation (Figure 4). The skeletal age, as measured by the standards of Gruelich and Pyle,[5] is in the range of 18 to 24 months, being closer to the latter standard. Figure 5 demonstrates accelerated skeletal maturation at age 11 years.

Comment

The radiographic findings in this patient are virtually specific for the diagnosis of pseudohypoparathyroidism. Shortened metacarpals and metatarsals may also be found in myositis ossificans progressiva, hereditary multiple exostoses, multiple epiphyseal dys-

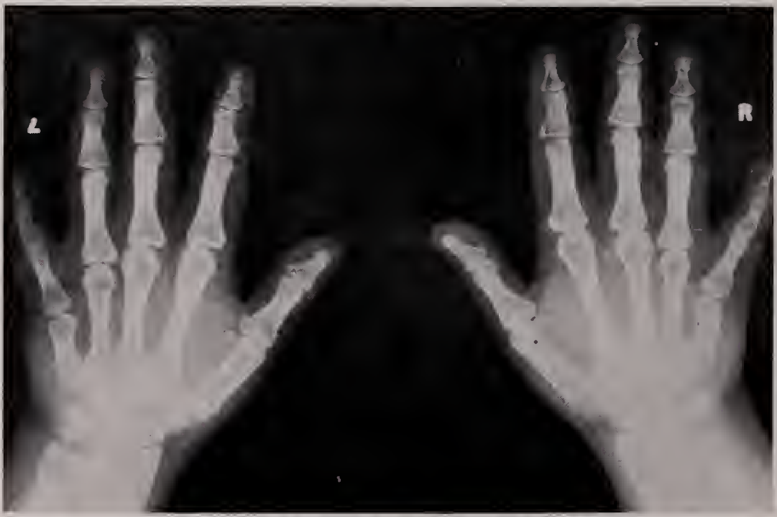

Fig. 1 — Age 27 years. Bilateral shortening and widening of the fifth metacarpals. Shortening of the fourth metacarpals.

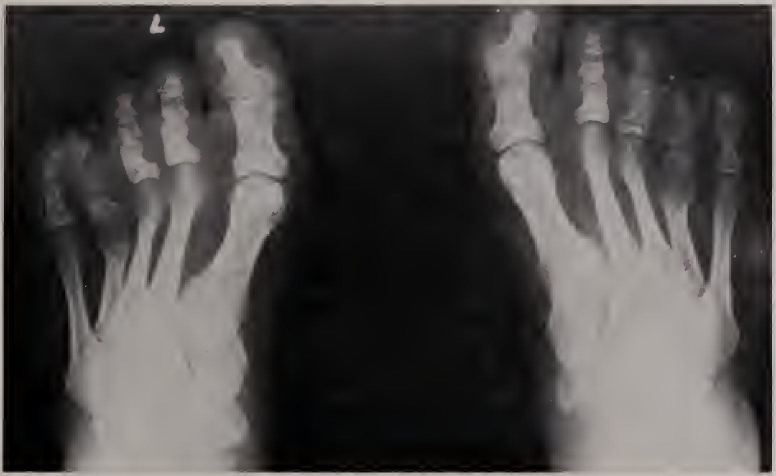

Fig. 2 — Age 27 years. Bilateral shortening and widening of the fourth metatarsals.

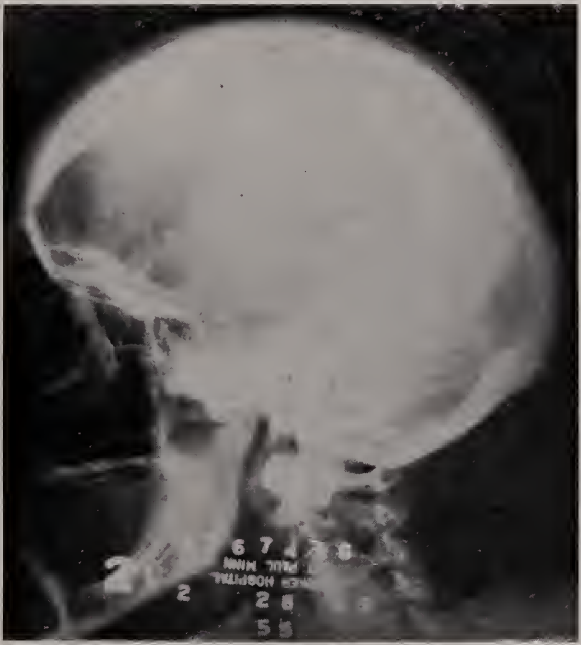

Fig. 3 — Age 27 years. Thickening of the calvarium due to widened diploic space.

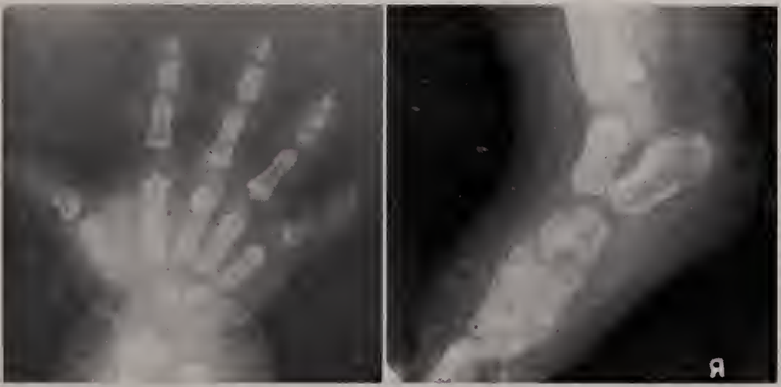

Fig. 4 — Age 11 months. Accelerated skeletal maturation is evident with the mean skeletal age estimated at 24 months.[5]

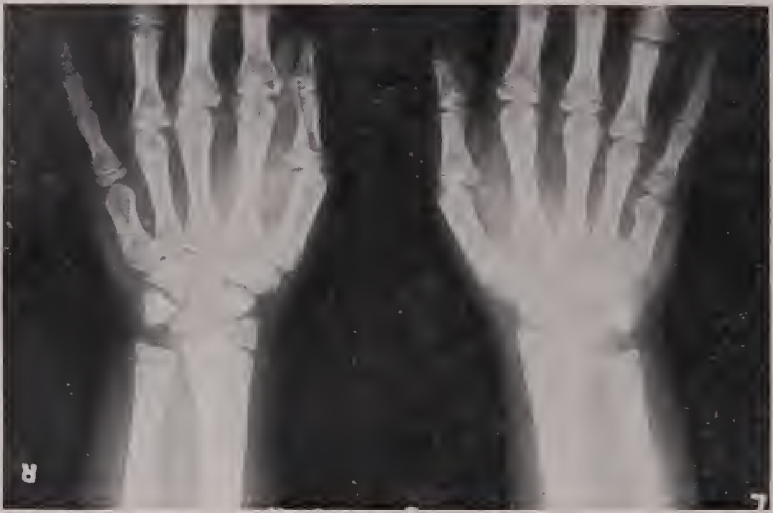

Fig. 5 — Age 11 years. Bilateral shortening and widening of the fifth metacarpals is evident. The epiphyses for the fifth metacarpals have closed.

plasia, and Turner's syndrome.[6]* However, thickening of the calvarium and accelerated skeletal maturation are specific among this group for the diagnosis of pseudohypoparathyroidism.

Except for the report of Cusmano,[4] there has been little emphasis on the finding of accelerated skeletal maturation. This was the earliest and most prominent finding in this patient, suggesting that pseudohypoparathyroidism must be included in the differential diagnosis of any child showing accelerated skeletal maturation.

Taitz[7] has described the case of a three-month-old infant with convulsions, tetany, hypocalcemia, and no response to a single intravenous dose of parathormone. The only radiographic finding was decalcification in the skull and long bones. Thus, the present patient represents (admittedly in retrospect) the earliest age of demonstration of the physical anomalies of this syndrome and also by far the longest follow-up of a verified case.

Mann[2] and Ray[8] explain the shortening of the metacarpals in this syndrome on the basis of premature closure of the epiphyses. However, Cusmano demonstrated shortening of the diaphyses during growth in his cases and stated that their metacarpal epiphyses did not fuse early. Our patient shows premature epiphyseal closure (Figure 5) ; however, the presence of widening of the shafts of the involved bones indicates a diaphyseal defect as well.

Because of the similarity in habitus and appearance of patients with hypothyroidism and pseudohypoparathyroidism, the former is frequently considered in the diagnostic work-up of these individuals. This patient represents the fifth documented case with both disorders.[9,10]

Summary

A case report is presented of a 27-year-old female exhibiting radiographic findings dating back to 11 months of age, the longest known follow-up on this syndrome. Accelerated skeletal maturation, thickening of the bony calvarium, and shortening of the metacarpals and metatarsals are emphasized in the diagnosis of this fascinating syndrome.

---

*See page 14.

We gratefully acknowledge the aid of David L. Hoffman, M.D., Section of Medicine, Mayo Clinic, Rochester, Minnesota, whose excellent diagnostic work-up on this patient provided the impetus for this report.

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ALBRIGHT'S SYNDROME

(Polyostotic Fibrous Dysplasia)

This syndrome may be discovered because of incidental or accidental finding of fibrous dysplasia of the bone or because of sexual precocity or because of brown pigmented areas of the skin which may be observed in the course of a routine checkup. The syndrome is usually observed in children or young adults, predominantly in females. Hereditary factors may account for the bone cysts.

The multiple bone cysts consist of fibrous dysplasia which replaces the medullary structure. It is found more often in pelvic bones and the bones of the lower extremities. On occasion it may not be recognized until a pathologic fracture has occurred in childhood or early adult life.

The accompanying areas of cutaneous pigmentation vary in size from freckle-like birthmarks to large, flat, brown patches. The degree of pigmentation signifies the extent of skeletal involvement.

The endocrine features consist of unusual sexual precocity in the female with early onset of menstrual cycle, enlargement of breasts, and development of adolescent external genitalia. The 17-ketosteroid values are normal.

It may be necessary to differentiate this condition from hyperparathyroidism in which the bone lesions are generalized, whereas in Albright's syndrome a considerable portion of the skeleton is usually unaffected.

Durham-Encyclopedia of Medical Syndromes
Hoeber, Inc., New York

Pliny[†] on Dentifrices

Dentifrices in the days of Pliny were made from deer horns, unburned and reduced to powder, or from the pastern-bone* of an ox reduced to ashes and mixed with myrrh, or from the ashes of burnt pigs' feet, or the calcined bone of the cotylid cavities in which the hipbones move. As a matter of fact, the pastern-bone of a she-goat just killed, or of any other four-footed beast reared in the farmyard, the bone being reduced to ashes, was considered to make an excellent dentifrice. In some instances nard** was added as a corrective for bad breath. "Some persons, however, think it a better plan to mix the ashes of a mouse's head with the dentifrice."

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*The phalanx of the ox though usually referred to the horse's foot.

**Used as perfume.

[†] See Minnesota Medicine, June 1964, page 716.

TURNER'S SYNDROME — (GONADAL DYSGENESIS)

The syndrome of ovarian dysgenesis is manifested typically by infantile development of secondary sex structures, short stature, and multiple congenital anomalies. Commonly associated anomalies are webbed neck, coarctation of the aorta, lymphedema of the extremities and skeletal, ocular and renal defects.

There may be iliac horns, dystrophy of the nails, anomaly of the patellae, and chondrodysplasia and arthrodysplasia, especially of the elbows. The iliac horns are occasionally found in routine roentgenograms and often indicate the presence of other abnormalities. Any one abnormality may occur independently of the others. Less constant abnormalities such as defects of the radial head, prominence of the acromion and clavicle, underdevelopment of the scapula, and discoloration of the iris have been reported.

Transmission occurs as a dominant hereditary character, and study of the genealogic tree of one patient revealed that 30 relatives in four generations exhibited these defects. (Senturia and Senturia).

Secondary sexual development is absent except for sparse pubic and axillary hair. The ovaries are replaced by a fibrotic ridge without evidence of either male or female germinal structures. A chromatin negative (male) sex-chromatin pattern is found in about 80 per cent of such patients. The typical finding in chromatin-negative gonadal dysgenesis is an XO sex chromatin constitution and a chromosome number of 45. In chromatin positive (female) dysgenesis two types of sex-chromatin abnormalities have been described: sex-chromatin mosaicism, and structural anomalies of the X-chromosome. Therapy is directed toward correction of the sexual infantilism and remediable congenital anomalies.

Grumbach, Melvin M.: Human Sex Anomalies from Cecil Loeb Textbook of Medicine, page 1421, Eleventh edition, W. B. Saunders, 1963.

WHAT'S YOUR DIAGNOSIS?

The patient was a clerk, age 30, intelligent, well educated. He had been ill for three months and was rapidly growing worse. Both hands were affected, the right more than the left. After writing for a short period of time the fingers would draw up in a cramped position, so that he could not use them. The fingers of both hands trembled a great deal, and he complained of severe numbness and shooting neuralgic pains in both. The index finger was very tender. He was unable to write a dozen lines, and yet he could paint and play the piano without difficulty. Prolonged effort to write produced cramps, jerking, and shaking, with the penmanship strokes becoming course and imperfect. A long rest of six months provided a cure.

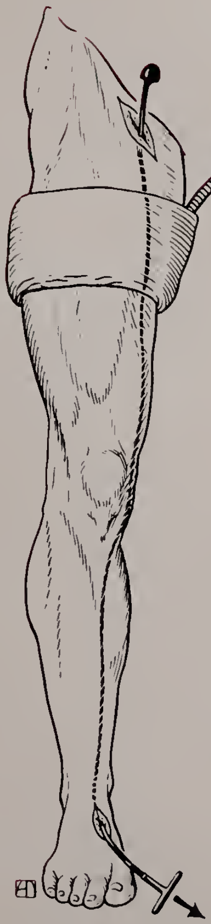
What's Your Diagnosis? Turn to page 21.

If common sense has not the brilliancy of the sun, it has the fixity of the stars.
—Caballero

Remember there's always a voice saying the right thing to you somewhere if you'll only listen for it.—Thomas Hughes

Varicose Vein Stripping in Bloodless Limbs

REINHARD FISCHER, M.D.
ROBERT D. LORGE, M.D.
Wattwil SG, Switzerland



APPROXIMATELY TWO years ago a bloodless operating field in the extremity was obtained when doing vein stripping by the use of a pneumatic tourniquet. This was proved to be satisfactory.

Method

Under general anesthesia the blood is removed from the leg by applying a tight rubber Esmark bandage from the toes to the thigh. The leg is then kept bloodless by placing a sterile pneumatic tourniquet in the mid-thigh with a pressure of 550 mm. of mercury. The Esmark bandage is then removed and the usual stripping procedure is performed. The stripper can be passed under the tourniquet. If the operation lasts longer than 90 minutes, the tourniquet is released for 10 minutes. The tourniquet is finally removed after the skin incisions have been closed and the leg has been wrapped with an elastic bandage.

Results

After a period of two years, 190 patients with a total of 312 limbs have been stripped of their varicose veins. In 98 patients the operation was done without tourniquet and in 92 patients with the pneumatic tourniquet. In the 98 patients where the tourniquet was not used, 71 required blood transfusions.

With Tourniquet

Of the 92 patients operated upon with tourniquet, four patients required transfusions.

Duration

Duration of the operation was an average of 69 minutes in those where tourniquet was not used, and 76 minutes when tourniquet was applied.

Postoperative Complications

There were no postoperative complications of any significance, and in the tourniquet group there was a loss of sensitivity in the distal part of the limb in two subjects. This symptom disappeared within a few hours.

Comments

It has been our observation that the operation can be done more thoroughly and accurately in a dry field, and there is no difficulty in isolating the veins because they are previously marked. With severe arterial disturbance the use of the tourniquet is inadvisable.

Reference

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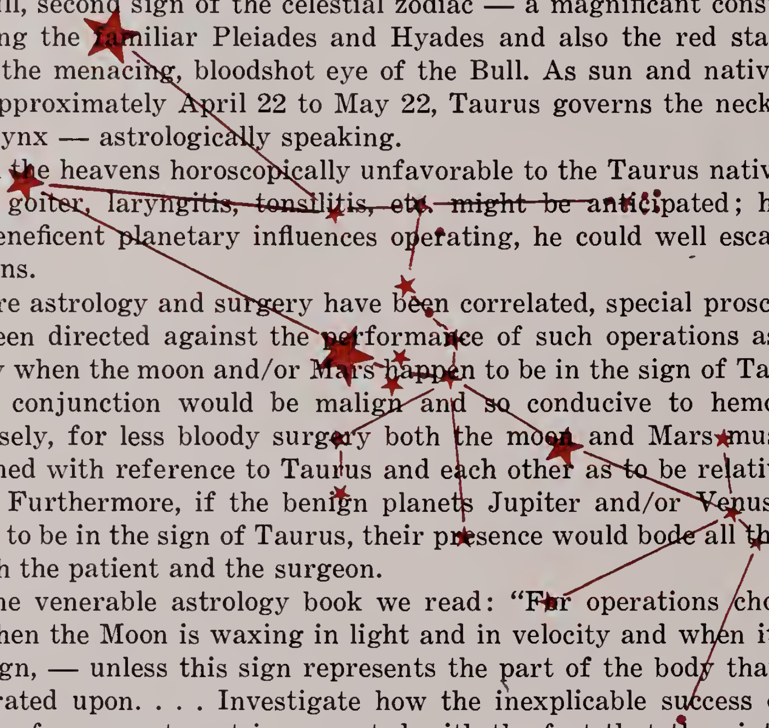
Astrology and Medicine — Taurus, the Bull



Brilliantly conspicuous in the southern January sky appears Taurus, The Bull, second sign of the celestial zodiac — a magnificant constellation including the familiar Pleiades and Hyades and also the red star, Aldebaran, the menacing, bloodshot eye of the Bull. As sun and nativity sign from approximately April 22 to May 22, Taurus governs the neck, throat and larynx — astrologically speaking.

With the heavens horoscopically unfavorable to the Taurus native, diphtheria, goiter, laryngitis, tonsillitis, etc. might be anticipated; however, with beneficent planetary influences operating, he could well escape such afflictions.

Where astrology and surgery have been correlated, special proscriptions have been directed against the performance of such operations as tonsillectomy when the moon and/or Mars happen to be in the sign of Taurus, as such a conjunction would be malign and so conducive to hemorrhage. Conversely, for less bloody surgery both the moon and Mars must be so positioned with reference to Taurus and each other as to be relatively impotent. Furthermore, if the benign planets Jupiter and/or Venus should happen to be in the sign of Taurus, their presence would bode all the better for both the patient and the surgeon.

In one venerable astrology book we read: "For operations choose the time when the Moon is waxing in light and in velocity and when it is in a fixed sign, — unless this sign represents the part of the body that has to be operated upon. . . . Investigate how the inexplicable success of some surgeons for a great part is connected with the fact that they intuitively choose the right time for their operations."*

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*C. Aq. Libra: Astrology: Its Technics and Ethics. Translated from the Dutch by Coba G. Published by P. Dz. Veen, Amersfoort (The Netherlands), 1917, p. 207.

Note: the present tense as used in this series, Astrology and Medicine, is the literary device known as the historical present.

There is no good in arguing with the inevitable. The only argument available with an east wind is to put on your overcoat.—Lowell

Isolation of Candidate Viruses in Hepatitis*

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H. SCHNEIDER, M.D.**
Detroit, Michigan

Broad co-operative studies can improve our knowledge of hepatitis. Present laboratory methods are successful and need wider application.

HEPATITIS REPRESENTS the major unresolved problem in blood banking today, particularly since knowledge concerning antigens and antibodies, technics for their identification and the application of preservative anticoagulant solutions have expanded to a very practical level. In the area of hepatitis, there is not only the hazard to recipients of blood as a medical complication but there is also the hazard to professional personnel due to medico-legal implications. Yet, from a public health standpoint, infectious hepatitis appears to be more common (over 70,000 cases are recorded annually). While the incidence of transfusion hepatitis remains uncertain, it appears to be considerably less than that of infectious hepatitis.

From the standpoint of this discussion, distinctions between infectious hepatitis due to Type A virus and transfusion hepatitis due to Type B virus will not be made since the technics to be mentioned are not able to make the distinction. From an investigative standpoint, information derived with respect to one viral agent will likely have a bearing on the other.

Candidate Agents

Primary emphasis is being placed on the isolation of candidate agents in hepatitis by several laboratories over the country. The candidate virus is one which is suspect as causative toward a disease. A number of such candidates have been reported in hepatitis. Most candidates at the moment are being derived by means of tissue culture technics. There are difficulties here, including 1) the fact that isolation of a transmissible agent in vitro does not imply an etiologic position, and 2) duplication of results in different laboratories has been difficult although some of these problems are being resolved.

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*Presented at the Annual Meeting of the Minnesota Association of Blood Banks, May 8, 1964, St. Paul, Minn.

**Department of Pathology and Blood Bank, Woman's Hospital and Wayne State University School of Medicine, Detroit.

Suitable Tissue for Culture

The hepatitis program at Wayne State University in Detroit has been directed primarily toward the development of a reliable technic for preparing primary cultures from various tissues suitable for propagating hepatitis candidates. By primary culture is meant a tissue culture from a normal source which can be reproduced, de novo, repeatedly from the original source and which is, at the same time, sensitive to candidate viruses of hepatitis. This term "primary" is used in contradistinction to an established cell line which is repeatedly transferred. In this connection, the reference tissue culture has been the Detroit-6Y (D-6) cell line first isolated by Stulberg and Berman from a patient having a malignant disease and used effectively by Rightsel, McLean and associates at the Parke, Davis Company. The Detroit-6Y line is an established cell line. It has been possible to maintain the line of Detroit-6Y cells highly sensitive to hepatitis candidates. In addition, cultures prepared from normal canine lung have shown great promise as means of transmitting the hepatitis candidates.

Library of Serums

The Wayne State University program has included a collection of serum from over 800 cases of hepatitis having classical, clinical expression including jaundice and evidence for self-limited, acute hepatocellular injury (elevated transaminase, thymol turbidity, gamma globulin, etc.). Acute and convalescent serums have been obtained from most cases. This library of serums is kept frozen and is being evaluated for candidate viruses as time allows.

Thus far, serum from over 120 cases has been evaluated for transmissible agents in tissue culture and has been found to be positive. The agents so recovered are stored in the frozen state. The harvesting of so many agents raises an obvious question, namely, the need for classification of the agents in order to determine whether few or many strains are involved. Already there is some indication that multiple strains pertain. Moreover, several laboratories have collected their own groups of candidate viruses. At present, a general attempt to classify these various agents appears most appropriate and germane. Unfortunately, the technics for classification are not simple and rest primarily on in vitro neutralization tests.

For the purposes of considering certain approaches used at Wayne State University, two major candidate viruses for hepatitis which we have isolated will be reviewed briefly. The cases from which these agents were recovered as well as a detailed account of the agents will be presented elsewhere.

Specific Agents

Several laboratories now have available cell lines which appear reasonably stable and sensitive to transmissible agents which can be derived from patients having hepatitis. Moreover, some laboratories at last are duplicating results from other laboratories. For instance, the two agents we are about to consider have been studied with comparable results at a preliminary level at two laboratories other than our own. The indications are then that with proper collaboration between research laboratories, it should be possible to delineate further the characteristics of the agents and to begin to consider more effectively the classification of different strains. Once pure agents are available, then the matter of more specific diagnostic tests can be tackled.

The technics at Wayne State University are well known classical tissue culture technics as applied to the recovery of viral agents. This includes the growth of monolayer cultures, the prevention of contamination with bacteria and fungi, and the demonstration of cytopathogenic effect as an index of positive growth of the transmissible agent or virus. Naturally, it must be demonstrated that the cytopathogenic effect is not due to a toxic ingredient used in the culturing technic. Thus, repeated cultures, repeated testings for contamination, and repeated testings for toxicity are necessary routines.

Concerning the technics of growth of cells sensitive to candidate agents in hepatitis, it was found that the cell line must be inspected daily and the media replenished as needed. The pH of the media is followed closely and the media is changed when the pH drops to 6.5. The cells are transferred at least twice a week and inoculated at approximately 80-100,000 cells per ml., thus keeping the tissue culture in the log phase of growth. The cell lines are handled in separate hoods which are used exclusively for a given cell line. This precaution became essential after five different cell lines were studied by R. R. A. Coombs for mixed agglutination. Three of the animal cell lines were found to be contaminated with human cells. A small hood was developed which prevented cross-contamination even after sixty transfers, as confirmed by chromosome studies.

Figure 1 shows a monolayer culture of Detroit-6Y cells prior to inoculation with a potential candidate material. The cells grow as a normal-appearing epithelial line (picture taken through a glass bottle). Figure 2 demonstrates the typical cytopathogenic effect. The cells have pulled away from each other, forming clear areas in the culture. At the same time, cells show definitive changes characterized by rounding of the cytoplasm, clumping of cells and alterations of nucleus.

Candidate Virus OE

The first exemplary case to be considered culminated in the isolation of dioxyribonucleic virus in the case of infectious hepatitis from serum and liver tissue of the patient. The agent has been labelled candidate virus OE after the initials of the patient, a 70-year-old white male who suddenly developed weakness, anorexia, chills, fever, nausea and vomiting ten days after moderate acute upper respiratory illness. He developed jaundice and within less than 36 hours was mentally confused and comatose. Liver function tests indicated severe hepatocellular damage, the coma worsened and the patient died. At autopsy, the liver was typical for acute yellow atrophy. Microscopically, there was also complete necrosis of the liver associated with collapse fibrosis, focal hemor-

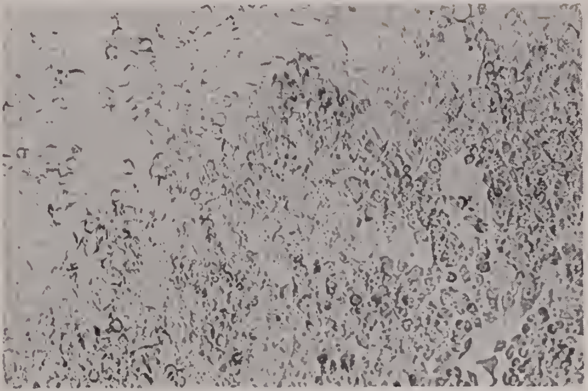

Fig. 1 — Regular (uninoculated) culture of Detroit-6 cell line, D_6Y clone.

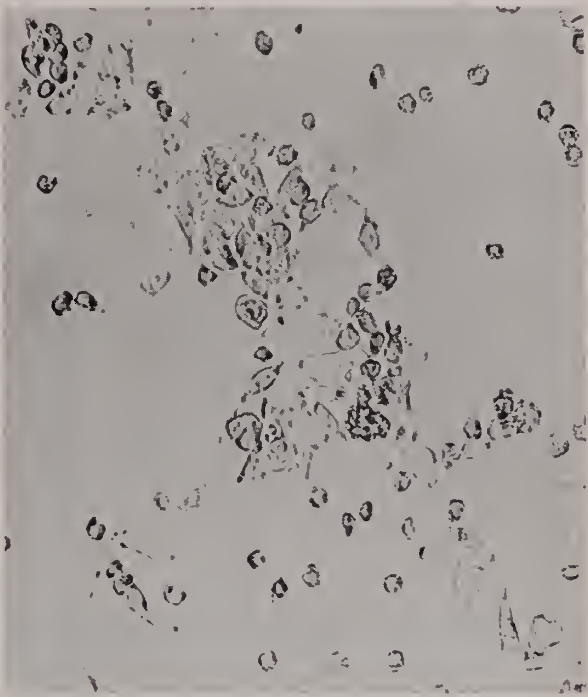

Fig. 2 — Cytopathogenic effect on D_6Y cell line as evoked by hepatitis candidate virus.

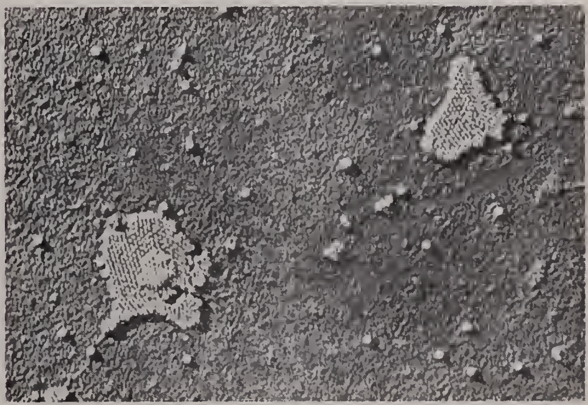

Fig. 3 — Viral-like particles from genetron extract of OE liver (electronmicroscopy by Dr. A. R. Taylor, Parke, Davis Company).

rhages and bile stasis. Other than hepatic findings, the patient exhibited only bronchopneumonia.

The tissue culture cells used for isolation purposes in this case consisted of a clone of Detroit-6Y cells which had been passed approximately 160 times and had retained uniform sensitivity to control hepatitis virus isolates of the candidate type. This particular cell line shows characteristic cytopathogenic effect within eight to 10 days. The control viruses were proved to be of hepatitis type by inoculation into normal volunteers as conducted by Boggs and the Parke, Davis Company.

The patient's acute phase serum was heated to 60° C for 30 minutes, then diluted 1:10, 1:20 and 1:40 in maintenance media and placed on the Detroit-6Y cells for primary isolation. Figure 1 shows representative cytopathogenic effect produced by this serum. These initial isolates were harvested and passed three times in Detroit-6Y cells and then stored for future study at −20° C.

Viral extracts were obtained from 2 gm. of candidate virus OE liver and from serum, using a modification of the Gessler method (fluorocarbon extraction). Aliquots of the supernatant from the genetron (fluorocarbon extraction) were used for virus isolation, nucleic acid identification and electronmicroscopy.

The extract was treated as a viral isolate and dilutions of 10^{-1}, 10^{-2}, 10^{-3} and 10^{-4} were made of material unheated and heated at 60° C in a water bath. Detroit-6Y cultures were inoculated. At seven days, typical cytopathogenic effect was noted. The extract of serum and of liver gave the same results. The 10^{-3} dilution was passed in the Detroit-6Y cells and subsequent titration of this second passage yielded a positive cytopathogenic effect through the 10^{-10} dilution, suggesting a major replication of the transmissible agent.

Two aliquots of the supernatant from the fluorocarbon extraction were treated with cold phenol. This phenol extract was subsequently treated with RNAse and DNAse and tested in the sensitive Detroit-6 cells. RNAse alone added to the maintenance media gave negative results (no cytopathogenic effect). The candidate virus OE nucleic acid plus DNAse gave negative results indicating that the material causing results originally was a dioxyribonucleic type virus. Conversely, the candidate virus OE nucleic acid subjected to RNAse gave positive results indicating that the material was not ribonucleic acid and by inference supported its dioxyribonucleic makeup.

A sample of the genetron supernatant was diluted 200 times in 0.1 normal Ringer's solution and subjected to electronmicroscopy

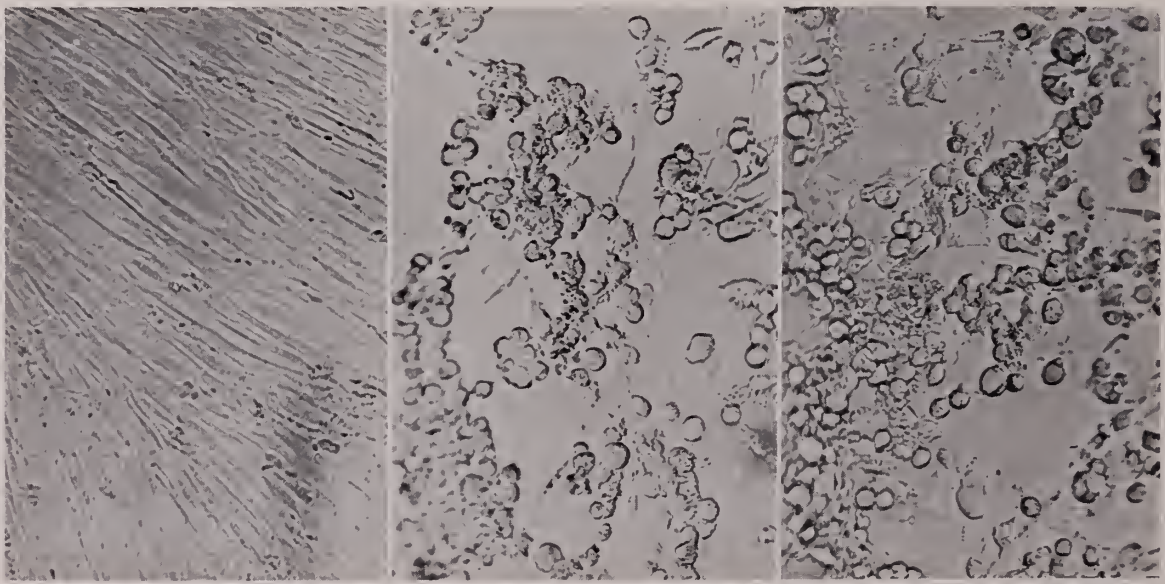

Fig. 4 — Canine lung cell line. Panel on extreme left represents uninoculated normal culture; the other two panels display CPE of canine line due to the RG agent.

by Dr. A. R. Taylor of Parke, Davis. Figure 3 shows representative viral particles from the candidate virus OE liver extract as derived by chrome shadowing.

In summary, patient with candidate virus OE exhibited a clinical and laboratory picture compatible with infectious hepatitis and acute yellow atrophy. The acute yellow atrophy was confirmed in autopsy. The serum from the patient as well as an extract of the hepatic tissue produced virus-like isolates which yielded typical cytopathogenic effect on Detroit-6Y cells indistinguishable from the cytopathogenic effect produced by control hepatitis virus as identified in a volunteer study conducted by Boggs and the Parke, Davis group. Further, the candidate agent appeared to be of dioxyribonucleic type.

Candidate Virus RG

The second agent we wish to consider was derived from a case of chronic hepatitis occurring in a young woman. This agent contrasts sharply in several respects with the candidate virus OE agent and therefore appears to be of a different strain. In addition, the agent has yielded interesting results with a primary cell line derived from the canine lung. The agent was derived repeatedly from the patient's serum. It has been designated as candidate virus RG from the initials of the patient.

The patient was first seen in 1959 at age 16 because of jaundice, light-colored stools, lassitude, epigastric pain. The liver was enlarged and tender. The laboratory findings included a serum bilirubin of 6 mg.%, and serum protein of 11 gm.% with 7 gm. of globulin. Three months later, the patient was readmitted with amenorrhea, arthritis, chills and fever. The bromsulphalein test was elevated and transaminase was greater than 500. Serum electrophoresis showed a total protein of 11.5 gm. with 8 gm. of gamma globulin of the broad base or polyclonal type. Biopsy of the liver was interpreted as showing chronic hepatitis or postnecrotic cirrhosis.

Candidate virus RG serum yielded positive cytopathogenic effect on the Detroit-6Y line. Figure 4 shows results with a primary canine lung line. The panel in the extreme left shows the appearance of the normal control canine line (uninoculated with candidate material). It grows as a fibroblastic line. The other two panels show the typical cytopathogenic effect as derived from the RG agent. There is rounding of the cells, clumping, and a characteristic ballooning effect of the cytoplasm due to vacuolization. Electronmicroscopy study of these cells conducted by Dr. Taylor showed particles within the cytoplasm which resembled viral particles. Earlier, there was some suggestion that the candidate virus RG agent resembled canine hepatitis virus and therefore may have activated a latent virus in the canine lung cells. Subsequent work has not supported this view. Thus, the candidate virus RG agent is considered as a candidate virus in hepatitis. It is unique in its characteristics in tissue culture as well as in its origin from a case of chronic liver disease in a young woman having the characteristics of the Bearn-Kunkel syndrome.

The types of observations made with the candidate agents OE and RG are similar to observations being made in different laboratories in this country. These include the recovery of viral-like agents from cases reflecting different types of hepatitis as well as from primates. Thus, the tools appear available for a fundamental elucidation of the etiology of hepatitis. These, however, need to be sharpened and there is additional need for a considerable amount of co-operative work at the level of interchange of information, technics and specific agents recovered.

ANSWER TO WHAT'S YOUR DIAGNOSIS

(From page 14)

This case was described by G. Durant Hood, M.D. in 1901 as being writer's cramp. It sounds like nothing in this modern age. What is your diagnosis?

Carpal Tunnel Syndrome*

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PAUL R. LIPSCOMB, M.D., F.A.C.S.***
EDWARD H. SOULE, M.D.†
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COMPRESSION NEUROPATHY of the median nerve in the carpal tunnel has been referred to by terms such as "acroparesthesia of the hand," "writer's cramp," "occupational neuritis," "partial thenar atrophy," "thenar palsy," "median neuritis," "median thenar neuritis," "tardy median palsy," and "carpal canal disease." This condition has become known as "carpal tunnel syndrome" because of the many causative factors, and controversy still exists concerning its etiology and pathogenesis. A clinicopathologic study was undertaken at the Mayo Clinic to determine the pathogenesis of this condition.

Material and Methods

This study is based on a review and analysis of data from 1215 patients with carpal tunnel syndrome seen at the Mayo Clinic from 1930 to 1960. These patients were seen from a few days to many years after the onset of symptoms. Eighty-four of the cases have been reported previously. Of the 1215 patients, 756 were treated nonsurgically or were observed after the diagnosis was made, and 459 patients were treated surgically. For the latter group, biopsy specimens and sections of tissue from 204 hands of 177 patients were available for study. The tissue sections were stained routinely with hematoxylin and eosin and in selected cases with a methyl violet stain for amyloid deposits. Several histologic sections from each specimen were studied.

The histories of all patients having carpal tunnel syndrome were reviewed carefully. Follow-up letters were sent to those who had been treated by surgical decompression, if follow-up studies were incomplete.

Controlled studies of the histologic material were based on gross and microscopic sections of the flexor synovialis and transverse carpal ligament obtained from upper extremities amputated because of malignant lesions.

Clinical Findings

Pertinent data concerning the age, sex and involvement of the hand are shown in Table 1.

The duration of symptoms before the patients were seen at this clinic varied from a few hours to forty years.

Categorization of the patients according to their occupations was somewhat difficult

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*Read at the meeting of the American Society for Surgery of the Hand, Miami Beach, Florida, January 25 and 26, 1963.

**Fellow in Orthopedic Surgery, Mayo Foundation.

***Section of Orthopedic Surgery, Mayo Clinic and Mayo Foundation.

†Section of Surgical Pathology, Mayo Clinic and Mayo Foundation.

Surgical correction of the compression found in "Carpal Tunnel Syndrome" provides relief from symptoms and prevents progression of the disease. Sensory and motor nerve loss can be prevented.

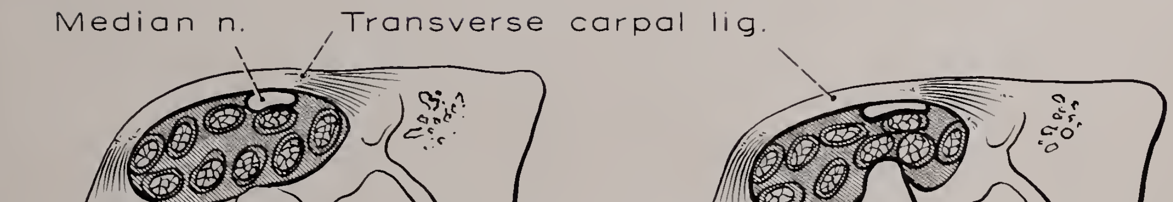

Fig. 1 — Mechanisms whereby the median nerve may be compressed in the carpal tunnel. (a) Normal relationship of the median nerve to the nine flexor tendons, tendon sheaths and transverse carpal ligament. (b) Encroachment of bone into the tunnel producing secondary compression of the nerve. (c) Thickening of the tendon sheaths (flexor synovialis) producing compression of the nerve. (d) Foreign bodies, tumors and other space-occupying lesions in the carpal tunnel producing compression of the nerve.

because many housewives had part-time jobs that were not listed in the clinical history (Table 2). Housewives (50.8 per cent) composed the largest occupational group; professional and sedentary workers (28.3 per cent) were the second largest group. Table 2 also shows the distribution of patients treated by surgical and nonsurgical methods.

TABLE 1
Age and Sex of Patients and Hand Involved

Age:	
Average, years	54
Range, years	16-90
More than 40 years, per cent	85
Sex:	
Females, per cent	69
Males, per cent	31
Ratio, females:males	2.25:1
Hand involvement, per cent	
Bilateral	56
Right	26
Left	18

Symptoms and Tests

Symptoms and signs of carpal tunnel syndrome are related to irritation, compression, or impairment of function of the median nerve at the wrist. The commonest symptoms were paresthesias (99 per cent of the 433 surgical patients); atrophy or weakness of the thenar muscle was noted in at least half of the patients. Electromyography proved to be of greatest value in our cases. The pneumatic-cuff test was performed in a few cases but was not helpful.

Associated Diseases and Trauma

Systemic diseases existed in 26.2 per cent of the 1215 patients, rheumatoid arthritis in 7.7 per cent, and myxedema in 6.3 per cent (Table 3). However, of the 318 patients with known systemic diseases, more than half (53.5 per cent) had rheumatoid arthritis or myxedema. Six had acromegaly. Sarcoidosis, polymyositis, syphilis, alcoholism, and neurofibromatosis were the only associated diseases in our series which had not been reported previously by other authors.

So-called rheumatic conditions were present in 237 or 19.5 per cent of our patients (Table 4). More than half (51.1 per cent) in this group had periarthritis of the shoulder. Traumatic conditions of the wrist were present in 161 or 13.2 per cent. More than half of this group had a history of Colles' or carpal navicular fractures; two had lunate dislocations; 66 had degenerative arthritis of the wrist not related to rheumatoid or other arthritis, and one had a hematoma of the wrist. Roentgenograms were made of 697 of the 1215 patients, and degenerative arthritis of the cervical portion of the spinal column was proved in 438 patients. Twenty-one were found to have asymptomatic cervical ribs. Eighteen had previously undergone operation elsewhere, eleven for carpal tunnel syndrome and seven for scalenotomy or cervical rib resection. One patient had a giant cell tumor on the distal portion of the radius.

TABLE 2
Classification of Patients by Occupation and Method of Treatment

Occupation	Surgical group	Nonsurgical group	Total Number	Total Per cent
Housewives	191	315	506	41.6
Housewives of farmers	38	74	112	9.2
Farmers	41	50	91	7.5
Professional and sedentary workers (doctors, dentists, nurses, nuns, accountants, clerks, teachers, salesmen, executives, stenographers)	132	212	344	28.3
Laborers (mechanics, carpenters, factory and construction workers, and common laborers)	43	61	104	8.6
Miscellaneous (waitresses, cooks, janitors, maids, bartenders)	14	44	58	4.8
Total	459	756	1215	100.0

Etiologic Aspects

Normally there is little room in the carpal canal, and any pathologic distortion of the wall or any conditions which increase the volume of the contents of the canal may produce carpal tunnel syndrome.

Commonly, the flexor synovialis becomes thickened owing to tenosynovitis associated with rheumatoid arthritis, gout, tuberculosis, pyogenic infections, myxedema, pregnancy, acromegaly and amyloidosis; but in the majority of cases carpal tunnel syndrome is due to nonspecific thickening of the tendon sheath. The altered relationship of structures in the carpal canal is illustrated schematically in a diagram similar to one prepared by Michaelis (Fig. 1).

Pathologic Findings

We compared the microscopic findings in specimens of the flexor synovialis removed from patients having carpal tunnel syndrome with similar specimens removed from amputated upper extremities of patients who, to our knowledge, had no history suggestive of carpal tunnel syndrome.

Specimens were obtained from a control group of fourteen patients whose ages varied from eleven to seventy-two years. Four were in the second decade, two each in the third, fourth, fifth, and sixth decades, and one each in the seventh and eighth decades.

No abnormality of the transverse carpal ligament was found in any of these specimens.

The test group of specimens consisted of tissue removed at the time of operation from 204 hands of 177 patients with carpal tunnel syndrome. There were twenty specimens of transverse carpal ligaments, and 204 specimens of flexor synovialis. Specimens from both wrists were not always removed from patients who had bilateral involvement.

Gross Observations.

Grossly, specimens from the controls exhibited a cloudy-white, nontransparent flexor synovialis of variable thickness in the older age group, whereas, in the younger age group this structure consisted of an extremely thin, glistening white, transparent membrane. The median nerve was not abnormal in any way in any of the fourteen controls.

In the test group gross examination of the median nerves at the time of operation showed them to be normal or flattened and constricted. At the point of constriction, the nerve was often hyperemic and there was increased fibrosis of the perineurium. Proximal to the constriction, there was apt to be

TABLE 3
Systemic Diseases or Conditions Associated With Carpal Tunnel Syndrome

Disease or condition	Patients, no.
Rheumatoid arthritis	93
Myxedema	77
Diabetes	69
Pregnancy	20
Amyloid deposits*	12
Raynaud's disease	7
Gouty arthritis	6
Acromegaly	6
Shoulder-hand syndrome	6
Tuberculosis	4
Disseminated L. E.	3
Sarcoidosis	3
Polymyositis	3
Syphilis	3
Alcoholism	3
Dermatomyositis	1
Polycythemia vera	1
Neurofibromatosis	1
Total	318

*Amyloid deposits were secondary to myeloma in six patients; in the other six patients deposits were idiopathic.

TABLE 4
Rheumatic Conditions Associated With Carpal Tunnel Syndrome

Condition	Patients, no.
Tennis elbow	13
Dupuytren's contracture	21
De Quervain's disease	15
Trigger fingers	26
Ganglion or cyst (wrist, knee, ankle and fingers)	24
Bursitis	
Trochanteric	8
Ischial	1
Olecranon	6
Periarthritis of shoulder (subdeltoid bursitis, bicipital tendinitis, calcific tendinitis, adhesive capsulitis)	121
Periostitis	1
Peyronie's disease	1
Total	237

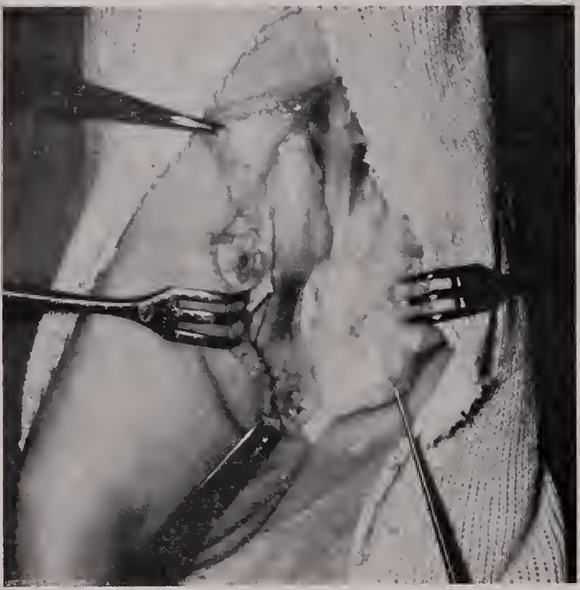

Fig. 2 — Note the severe constriction of the median nerve in a patient with long-standing carpal tunnel syndrome due to thickened flexor synovialis. A neuroma had formed proximal to the point of constriction. Hyperemia had also developed at this point. Thenar atrophy and sensory loss were present in this patient. (From Lipscomb, P. R.: Tenosynovitis of the Hand and the Wrist: Carpal Tunnel Syndrome, de Quervain's Disease, Trigger Digit. Clin Orthop 13:164, 1959).

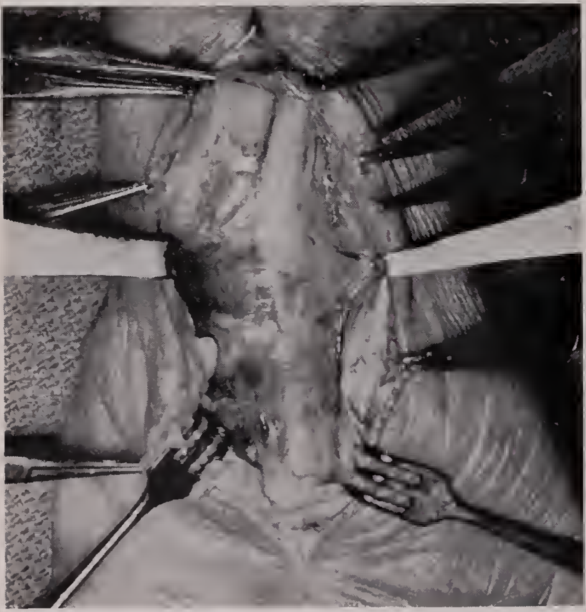

Fig. 3 — Exposure of the median nerve in the carpal tunnel. The flexor synovialis is grossly inflamed and thickened. The increased vascularity, the edema of the synovia and the crowding within the carpal tunnel completely obscure the flexor tendons.

fusiform enlargement of the nerve. The flexor synovialis was thickened, cloudy white, nontransparent and lusterless; variable amounts of edema and fluid were present. If inflammation was present, the synovialis appeared gray, thickened, hyperemic, and edematous and an increased amount of fluid was present (Fig. 2 and 3).

Microscopic Observations

Microscopically, the control group of specimens showed the presence of one to five layers (depending on the age group) of flattened endothelial-like cells in the synovium (Fig. 4 and 5). Next appeared a layer of subsynovial tissue (zone 2) (Fig. 4 and 5), which consisted of loose areolar tissue having few capillaries, and then a dense layer of collagenous, fibrous tissue with scattered fibroblasts and arterioles (zone 3). Usually a layer of fatty tissue was present at the periphery (zone 4).

In the older age group, zone 1 was as thick as five cell layers, while zones 2 and 4 remained about the same in thickness, depending somewhat on the obesity of the patient. Zone 3 showed the greatest difference in the controls. In the older age group the degree of fibrosis and thickness of the vessel walls was increased. Rarely were inflammatory cells present in any of the four zones.

Histologic Grading

For the most accurate comparison of the findings in the controls with those in the test specimens removed from surgical patients, a more detailed list of factors was examined. Histologic sections were evaluated by rating the relative presence or absence of ten factors. Each factor was graded from 0 to 4: zero indicated an absence of the factor, grade 1 slight presence, grade 2 moderate presence, grade 3 rather definite presence, and grade 4 considerable evidence of the factor.

The ten factors studied in the varying zones were as follows: *zone 1:* (1) synovial layer (number of cell thickness), (2) synovial folds or villi; *zone 2:* (3) quantity of subsynovial capillaries, (4) amount of edema; *zone 3:* (5) quantity of subsynovial capillaries and arterioles, (6) thickness of walls of blood vessel, (7) degree of subsynovial fibrosis; *zone 4:* (8) amount of adipose tissue; and in *zones 1 to 4:* (9) inflammatory cells (lymphocytes, plasma cells, monocytes and polymorphonuclear leukocytes) and (10) amount of perivascular inflammatory cells.

Pathologic findings were classified in two main categories: (1) well-defined, or (2) ill-defined and not fitting into the pattern of any previously described entity.

In the group in which the pathologic findings were well-defined, twenty-two patients had specimens compatible with a diagnosis of rheumatoid tenosynovitis: two with gouty tenosynovitis and one each with lipoma, neuroma (following previous operation), suture granuloma, amyloidosis, nonspecific granulomatous tenosynovitis, tuberculous tenosynovitis and an isolated bony ossicle (Fig. 6 and 7). The etiology of the carpal tunnel syndrome in these patients was easy to establish and therefore no further elaboration is required. This group composed only 17.5 per cent of the 177 patients whose tissue was analyzed. Carpal tunnel syndrome in 12.4 per cent of this group was due to rheumatoid tenosynovitis.

The specimens from 146 patients fell into the category of ill-defined findings with a pattern that did not fit any previously described entity; specimens from the 146 patients (71.8 per cent) were thought to show nonspecific tenosynovitis and were classified according to microscopic findings into the following four subgroups.

Subgroup 1

Nineteen patients (10.7 per cent of 177) with findings similar to the control group were called "normal" and compared favorably with the control group (Fig. 5).

Subgroup 2

Sixty-two patients (35 per cent) with findings only slightly more significant than those of subgroup 1 showed a slightly greater amount of fibrosis and edema; occasionally inflammatory cells were noted (Fig. 8*a*).

Subgroup 3

Forty patients (22.6 per cent) in whom the findings differed greatly from those in subgroups 1 and 2: zone 1 was thickened and consisted of six to ten cell layers, zone 2 was much more vascular, zone 3 showed an increase in fibrosis and thickened vessel walls. Inflammatory cells were present in moderate amounts in nearly all zones but especially in zones 2 and 3 (Fig. 8*b*).

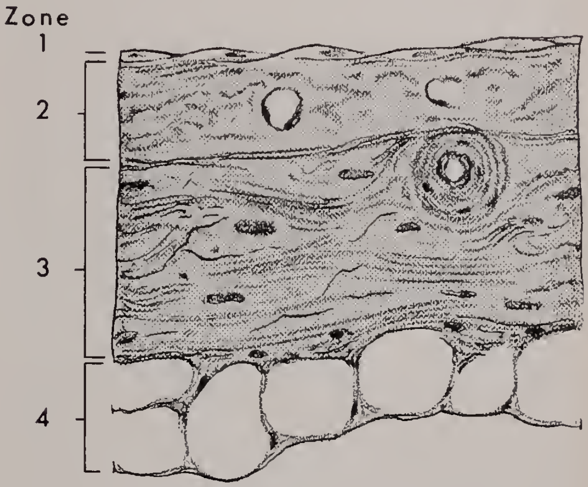

Fig. 4 — Diagram of normal histologic section of the flexor synovialis. The tissue layers are denoted as zones: zone 1, endothelial-like cells; zone 2, loose areolar tissue; zone 3, fibrous tissue with scattered fibroblasts and arterioles; and zone 4, fatty tissue.

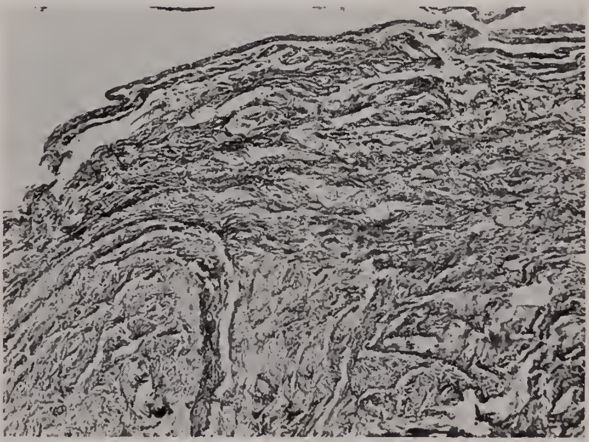

Fig. 5 — Section of the flexor synovialis of a twenty-nine-year-old person from the control group. The synovial membrane is two cell layers thick, beneath which is rather avascular subsynovial fibrous tissue (hematoxylin and eosin; magnification x95 before reduction).

Subgroup 4

Twenty-five patients (14.1 per cent) with severer findings than those in subgroup 3: zone 1 was greatly thickened and was often infiltrated with inflammatory cells. In certain areas the cell reaction and vessels were so numerous that the tissue simulated a hemangioma or granulation tissue (Fig. 8*c* and 9).

Diagnosis

The following factors should be considered in the diagnosis of carpal tunnel syndrome: (1) a history of paresthesias in the distribution of the median nerve, (2) a history of major trauma, (3) a history of associated systemic diseases or conditions, (4) objective sensory impairment in the distribution of the median nerve, (5) weakness or atrophy of the thenar muscles, (6) localized swelling proximal to the distal wrist crease, (7) tenderness or tenseness in the region of the transverse carpal ligament, (8) vasomotor or trophic changes in the hand, (9) positive results to the wrist flexion test of Phalen, (10) positive Tinel sign, (11) positive results to the tourniquet test of Gilliatt and Wilson, and (12) amelioration of symptoms with immobilization of the wrist in the neutral position by light plaster-of-paris splint and by the injection of hydrocortisone into the carpal canal.

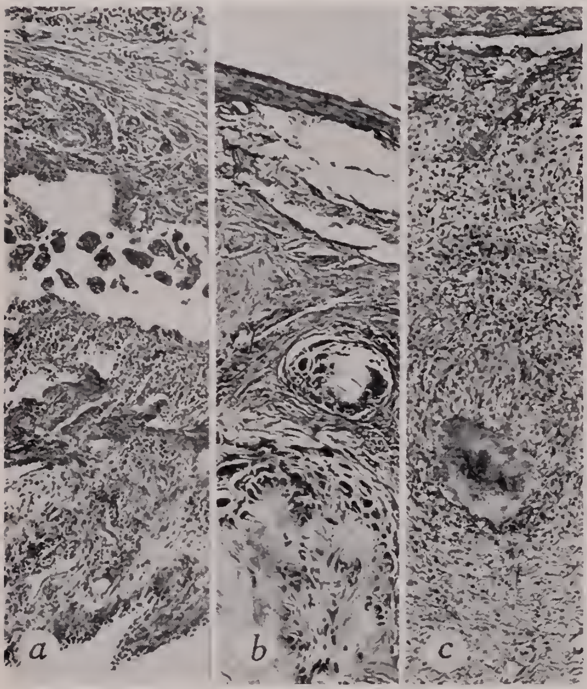

Fig. 6 — Specific types of tenosynovitis: (a) Section of the flexor synovialis from a sixty-year-old woman with rheumatoid tenosynovitis. Note the definite villous formation and the diffuse infiltration of inflammatory cells about the vessels and in the subsynovial tissue (hematoxylin and eosin; magnification x65 before reduction). (b) Section of the flexor synovialis from a patient having gouty tenosynovitis. Note the thin synovial layer on the top and the uric acid deposit on the bottom surrounded partly by foreign body giant cells (hematoxylin and eosin; magnification x100 before reduction). (c) Section of the flexor synovialis from a twenty-seven-year-old man with nonspecific granulomatous tenosynovitis. Note the giant cell in the center of the granuloma (hematoxylin and eosin; magnification x100 before reduction). Tissue cultures for fungi and tubercle bacilli were negative.

Laboratory Aids

Aids to establishment of a diagnosis include electromyography with delayed conduction time in the fibers of the median nerve across the carpal tunnel (Fig. 10) and roentgenograms to show whether evidence of degenerative arthritis, old fractures, extra ossicles, or other changes appears at the wrist joint. Myxedematous patients show a decrease in protein-bound iodine, radioactive uptake, and basal metabolic rate. Patients with rheumatoid arthritis may have an increase in the erythrocyte sedimentation rate and a positive rheumatoid factor.

Evidence of Nerve Damage

Although thenar atrophy and paresthesias and sensory loss in the distribution of the median nerve can each occur with other disease entities, this combination of symptoms and signs is unlikely to be found in nontraumatic conditions other than carpal tunnel syndrome.

Paresthesias in the fingers due to protruded cervical disks or cervical spondylosis are generally accompanied by radicular features and associated with pain and limited motion in the neck.

In our series of 1215 patients, an interval of two weeks to twenty years was noted between the onset of involvement in the dominant hand and the involvement of the other hand.

Treatment

Marie and Foix in 1913 first suggested treatment of the carpal tunnel syndrome by sectioning of the transverse carpal ligament. This was first carried out in 1941 on a patient at the Mayo Clinic.

Surgical Decompression

Longitudinal section of the transverse carpal ligament is still the treatment of choice for most patients with appreciable trouble from carpal tunnel syndrome. General anesthesia, axillary block, or local anesthesia may be used for the procedure. A bloodless field is provided by the use of a tourniquet on the upper part of the arm. The section is always carried to the ulnar side of the nerve. It is advisable (as advocated by Phalen) to section the palmaris longus tendon and to allow it to retract upward.

Of the 459 surgical decompressions in our series, 62.7 per cent of the patients had bilateral operations; 24.2 per cent had operations on the right hand only, and 13.1 per cent on the left hand only. *Neurolysis* usually was performed if the median nerve was constricted. Hydrocortisone was injected into the carpal tunnel in most cases at operation. Ninety-six per cent of the patients had good sensory recovery and 50 per cent had improvement in thenar muscle function after operation, the degree of sensory and motor recovery depending on the duration of symptoms and the severity of involvement. In general, sensory recovery was good, with improvement over a period of months. If thenar atrophy had been present for longer than a few weeks there was little recovery of motor function.

Desiccated Thyroid

Patients with myxedema generally responded to conservative treatment with desiccated thyroid; but surgical decompression was performed on eight of seventy-seven patients with myxedema because of progressive and incapacitating symptoms and weakness of the thenar muscle.

Splinting

Splinting of the wrist in patients with nocturnal symptoms who had no objective sensory loss or thenar atrophy was efficacious in a number of patients. Hydrocortisone injected into the carpal canal also gave temporary relief of symptoms early in the course of the syndrome.

It was noted that symptoms of the carpal tunnel syndrome which appeared in the last trimester of pregnancy usually subsided spontaneously within a few weeks or months after delivery. Of the twenty pregnant women suffering from this syndrome in our series, only one needed surgical decompression. This was carried out four days after delivery because of objective loss of sensation and severe paresthesias in the distribution of the median nerve.

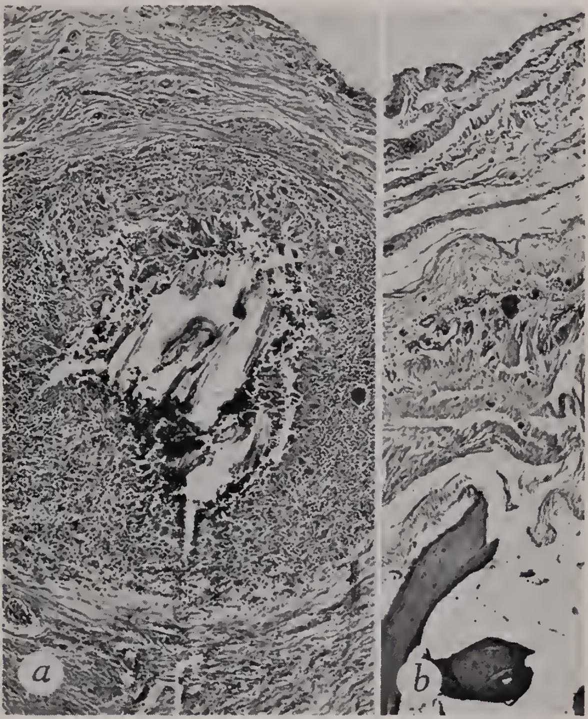

Fig. 7—(a) Section of the flexor synovialis from a fifty-seven-year-old woman who had had a previous surgical decompression elsewhere six months previous to coming to the clinic for carpal tunnel syndrome and who had recurrence of symptoms. Note the focal, subacute, and chronic microabscesses with foreign body giant cell and suture material (hematoxylin and eosin; magnification x70 before reduction). (b) Section of flexor synovialis from a fifty-seven-year-old man who had tenosynovitis and carpal tunnel syndrome due to an osseous body lying in the carpal canal. Note the slightly thickened synovium at the top on the left and the osseous trabeculae at the bottom (hematoxylin and eosin; magnification x50 before reduction).

Results

At the time of this report the recurrence of symptoms after operation in our series has been very low. Only three of the patients on whom we operated have required more than one operation on the wrist; eleven others had had surgical decompression performed previously elsewhere. Thirteen patients were thought to have had inadequate decompression at the time of the first operation, and the recurrences may have been due to inadequate sectioning of the distal fibers of the transverse carpal ligament. A wound infection developed in one of our patients after the first surgical procedure, and at the second operation the nerve was found in dense scar tissue which no doubt resulted from the infection. This patient obtained excellent relief of symptoms after neurolysis.

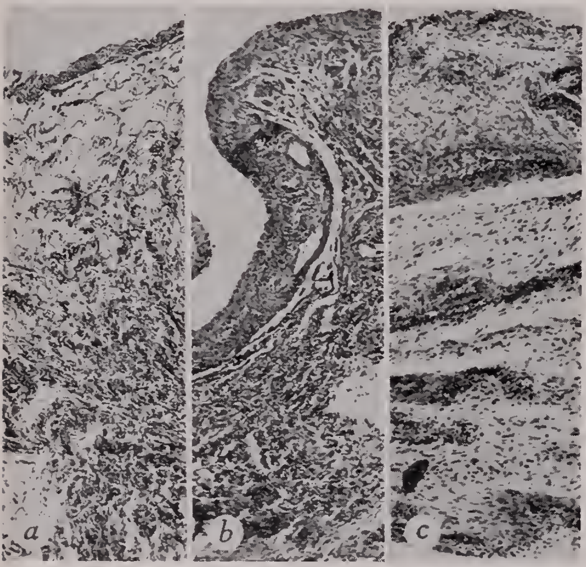

Fig. 8—(a) Section of the flexor synovialis from the carpal canal of a fifty-four-year-old woman with carpal tunnel syndrome, demonstrating mild nonspecific tenosynovitis. Note that the synovial membrane is slightly thickened and that the subsynovial tissue shows mild increase in fibrous tissue and a small amount of edema (hematoxylin and eosin; magnification x100 before reduction). (b) Section of the flexor synovialis of a fifty-year-old-woman demonstrating moderate nonspecific tenosynovitis. Note the thickened synovial layer, increased vascularity and moderate numbers of inflammatory cells in the subsynovial tissue (hematoxylin and eosin; magnification x95 before reduction). (c) A section of the flexor synovialis from a fifty-four-year-old woman demonstrating marked nonspecific tenosynovitis. Note the thickened synovial layer and increase in fibrous tissue and inflammatory infiltrate along the vessels and in the subsynovial layer (hematoxylin and eosin; magnification x75 before reduction).

Comment

The earliest symptoms are related to autonomic dysfunction and are poorly localized; they consist of vague sensations of discomfort in the hand. As the condition increases in severity, the patient complains of swelling, tightness, and redness of the hand. In the past these symptoms were referred to as "acroparesthesiae"; sometimes they extend into the forearm and occasionally into the upper part of the arm.

Paresthesias

The paresthesias are experienced first at night and later during the day. During the day most patients experience symptoms intermittently when using the hand. Symptoms seem to lessen during vacations with inactivity and rest and to worsen after a hard, long day of work or sometimes during cold weather.

When continuous hypesthesia or anesthesia occurs, patients become aware of impaired tactile discrimination in the fingers, and fine movements of the fingers are performed clumsily and with difficulty.

Atrophy and Weakness

With pain and weakness of the thenar muscle, a decrease in power of grip and an inability to grasp articles is manifested. Atrophy of the thenar muscles is a comparatively late finding in most cases and is accompanied by impaired opposition of the thumb. In far-advanced stages of carpal tunnel syndrome, atrophy of the thenar muscles produces a characteristic grooving of the thenar eminence (Fig. 11). Thenar wasting antedated dysthesia in fifteen patients in our group.

Vasomotor Disturbances

Vasomotor disturbances such as Raynaud's phenomenon, trophic ulcers and differential sweating in the palm and finger tips are encountered with carpal tunnel syndrome.

*Brachial Plexus Syndrome**

The thoracic outlet syndromes are not as common as was once thought. Many cases of carpal tunnel syndrome were at one time mistaken for thoracic outlet syndrome. Seven patients in our series had had scaleniotomy or cervical rib resection previously without relief of their original symptoms of paresthesias. It is now realized that obliteration of the radial pulse on Adson's maneuver does not necessarily indicate that paresthesias are due to a thoracic outlet syndrome. Roentgenograms showed evidence of asymptomatic cervical ribs in twenty-one of 697 of our patients.

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*See page 34.

Compression of Median Nerve

Compression of the median nerve between the two heads of the pronator teres during its passage into the proximal forearm or at the site of a supracondylar process of the humerus rarely produces symptoms similar to those of carpal tunnel syndrome. The presence of fatty connective tissue in the carpal canal of obese patients, and the fact that the carpal canal is smaller in females than in males, may help to explain the predilection for compression of the median nerve in females. Tanzer stated that heredity and anatomic abnormalities are predisposing factors. Congenital anomalies such as an anomalous median artery, anomalous sublimis slip in the carpal canal and anomalous pathway of the motor branch of the median nerve through the transverse carpal ligament are rare causes of carpal tunnel syndrome. Many authors have shown that flexion and extension of the wrist result in increased pressure within the carpal canal.

Lower Motor Neuron Lesions

Occasionally, thenar atrophy is associated with lesions of the lower motor neuron such as anterior poliomyelitis or progressive muscular atrophy. In the former, the entire thenar group of muscles including both heads of the flexor pollicis brevis muscle is involved, and there is no sensory loss; in the latter, all the intrinsic muscles of the hand are generally involved.

Other conditions such as tumors of the spinal cord, syringomyelia, subacute combined degeneration, multiple sclerosis, degenerative disease of the spinal cord, amyotrophic lateral sclerosis, polyneuritis, local lesions involving the brachial plexus or cervical roots, aneurysm of the subclavian artery, and brain tumors can produce weakness and paresthesias of the hand. The diagnosis usually can be made after a detailed neurologic examination if one keeps in mind the anatomy of the involved extremity. Electromyography is the best aid for distinguishing most neurologic conditions from carpal tunnel syndrome.

Peripheral Vascular Disease

Some writers have considered ischemia to be important in the pathogenesis of the syndrome. We found a greater degree of peripheral vascular disease associated with the

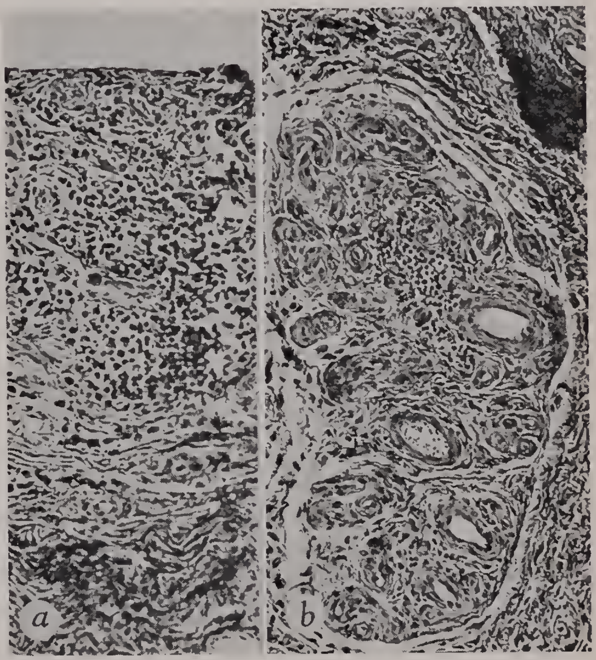

Fig. 9 — (a) Section from the flexor synovialis of a fifty-five-year-old man with severe marked nonspecific tenosynovitis. Note the greatly thickened synovial layer infiltrated with lymphocytes and plasma cells (hematoxylin and eosin; magnification x200 before reduction). (b) Section from the flexor synovialis of a thirty-eight-year-old woman with marked nonspecific tenosynovitis. Note the thickened synovial layer in the upper right hand corner. This section demonstrates the greatly increased vascularity simulating granulation tissue or hemangioma; there are moderate numbers of inflammatory cells around the blood vessels and some increase in fibrous tissue in the subsynovial tissue (hematoxylin and eosin; magnification x160 before reduction).

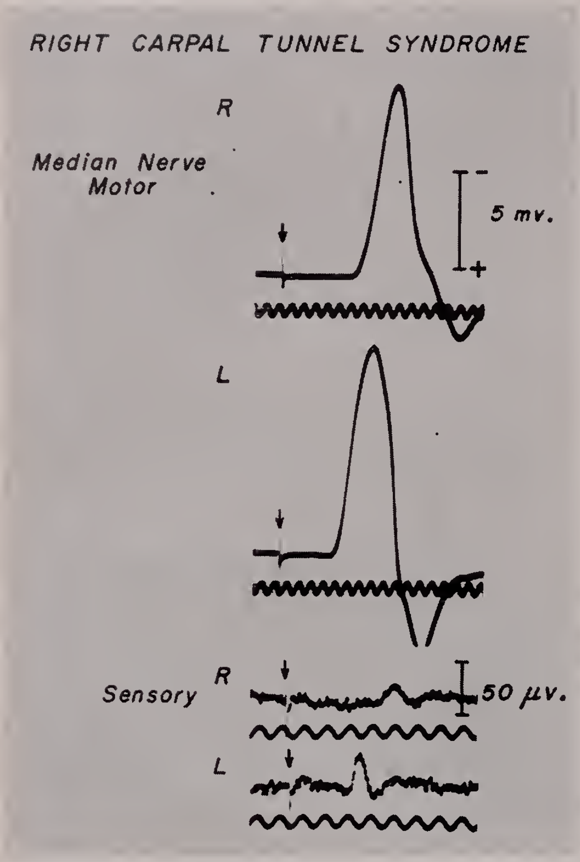

Fig. 10 — Electromyograms in the top two tracings show the action potential of the thenar muscles from stimulation of the median nerve at the wrist joint proximal to the carpal tunnel. The initial artifact (at the arrow) indicates the beginning of the electric stimulation. The gross wave shows the muscle potential. Each small wave represents one millisecond (1/1000 sec.).

In the right (R) hand the latency, from the artifact to the beginning of the action potential, is prolonged to 5.9 milliseconds (ms.). The left (L) hand has a latency of 4.3 ms. The upper limit of normal is 4.7 ms.

The first tracing of the right side shows a height of 5 millivolts on the top tracing and 50 microvolts on the bottom tracing. The bottom two electric tracings show the action potential of the sensory aspect of the median nerve from the tip of the index finger to the proximal part of the carpal tunnel at the wrist joint. The latency of response is 4.8 ms. on the right and 3.2 ms. on the left. The upper limit of normal is 3.5 ms. The velocity of nerve conduction from the elbow to the wrist joint was normal (R = 52 meter/sec.; L = 54 meter/sec.). (From Thomas, J. E., and Lambert, E. H.: Das Karpaltunnelsyndrom. München Med Wschr 104:123, 1962).

aging process and with diabetes (69 cases in our series). This finding was demonstrated in our microscopic examinations by an increased fibrosis around the small vessels in the subsynovial layer of the flexor synovialis and was noted in the control group and in most of the older patients having the carpal tunnel syndrome.

Physiologic Aging Process

From our study it was found that an aging process results in thickening of the flexor synovialis because of increased fibrosis and degenerative phenomena. It may be that occupational microtrauma enhances the aging process. As mentioned previously, 85 per cent of the patients with carpal tunnel syndrome in our series were more than forty years of age.

An association of the syndrome with certain "rheumatic conditions" was noted to occur in almost 20 per cent of the patients in our series (Table 4). It may be that in such patients the reaction of their connective tissue to trauma or other stimuli is altered. It has been postulated that estrogen deficiency plays a part in the production of nonspecific tenosynovitis and so-called rheumatic conditions. If such were the case, this might help to explain the preponderance of cases of carpal tunnel syndrome in women after menopause.

The group of 146 patients in our series with proved nonspecific tenosynovitis (sixty-five marked or moderate) adequately explains the production of symptoms on the basis of median-nerve compression in the carpal canal as a result of disproportion between contents and space. In sixty-two patients with only mild nonspecific tenosynovitis and in nineteen with normal flexor synovialis, a logical question is: Was the proliferation of the flexor synovialis in these patients sufficient to cause secondary compression of the nerve in the tight tunnel? In the control group as well as in 146 patients with proved nonspecific tenosynovitis, perhaps the degenerative process which produced thickening of the flexor synovialis contributed to compression of the median nerve, although it was normal for the older age group.

Summary and Conclusions

A clinicopathologic study was made of 1215 patients with carpal tunnel syndrome seen at the Mayo Clinic from 1930 to 1960. Of the 1215 patients, 756 were treated nonsurgically or were observed, and 459 were treated surgically.

The average age of the patients was 54 years; 85.3 per cent were more than forty years of age. The ratio of females to males was 2.25:1 and more than half of the patients were housewives. Bilateral carpal tunnel syndrome was present in 56.1 per cent of the patients, 26.1 per cent had involvement only on the right side, and 17.8 per cent involvement only on the left side. Patients had had symptoms for a few hours to forty years before they were seen at the Mayo Clinic.

The commonest clinical findings were paresthesias, thenar atrophy or thenar muscle weakness, positive results to Phalen's test, and positive Tinel's sign. Thickening of the flexor synovialis was noted grossly in almost every patient operated on for carpal tunnel syndrome. Microscopically, the flexor synovialis revealed varying degrees of nonspecific tenosynovitis in 71.8 per cent of the studied cases. Usually it was traced to a degenerative process that occurred with aging or systemic disease.

Early surgical decompression of the carpal tunnel by sectioning or resecting part of the transverse carpal ligament is highly successful in preventing progression of the symptoms and signs due to compression of the median nerve in the carpal canal. Permanent sensory and motor loss may follow prolonged compression of the median nerve in the carpal canal. Recurrence is rare after surgical decompression of the median nerve.

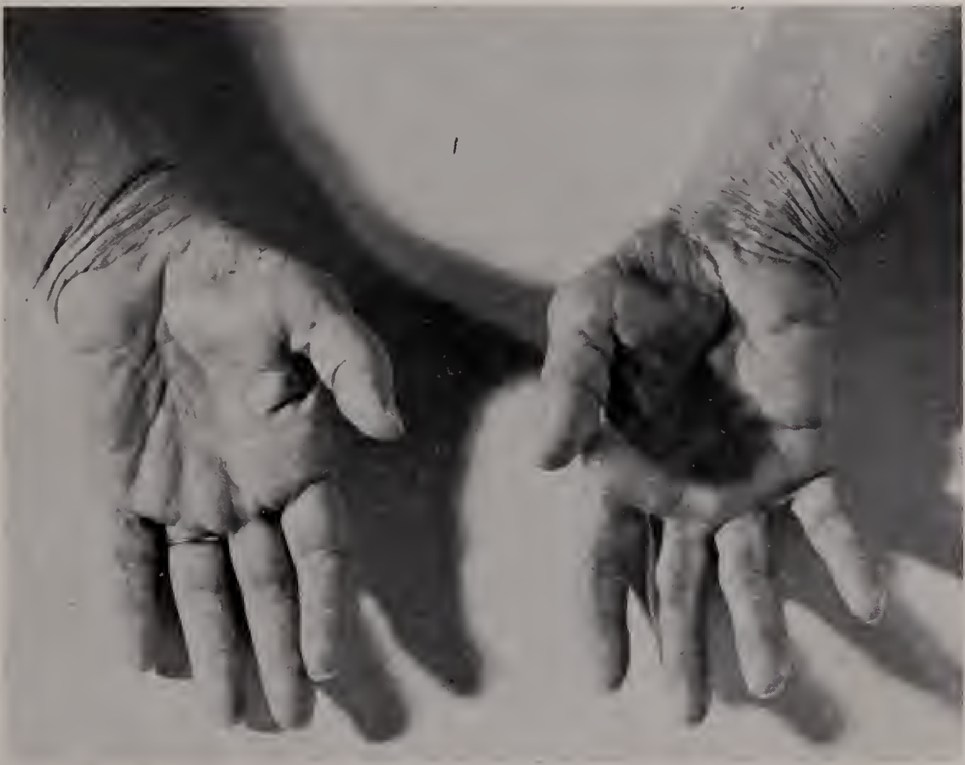

Fig. 11 — The hands of a patient having bilateral carpal tunnel syndrome with thenar atrophy. Note that the abductor pollicis brevis muscle is primarily involved but the flexor pollicis brevis is not greatly atrophied. The result is a shelflike appearance of the thenar eminence.

BRACHIAL PLEXUS SYNDROME

(Scalenius Anticus Syndrome) (Haven's Syndrome)

The brachial plexus syndrome results from the mechanical narrowing of the thoracic outlet space, causing pressure or torsion on the vessels and nerves supplying the upper extremities. There may be a considerable number of mechanical factors or anatomic deviations to cause this. The compression may be on the nerve, causing peripheral nerve disturbances with atrophy, pain, weakness, etc., or it may be on the artery, causing impaired circulation to the upper extremities.

Resection of the scalenius anticus tendon does not always provide benefit. It has been recommended by some authors that conservative and postural exercises be used before recommending surgical operation.

Durham's Encyclopedia of Medical Syndromes. Hoeber, Inc.

IT'S THE LAW

Physicians and Surgeons Prohibited from Splitting Fees

It shall be unlawful for any physician or surgeon to divide fees with, or to promise to pay a part of his fee to, or pay a commission to, any other physician or surgeon or person who calls him in consultation or sends patients to him for treatment or operation.

Punishment for Violation

Any physician or surgeon who pays or receives any money prohibited by section 147.11 shall be punished by a fine not to exceed $100.00, or by imprisonment in the county jail for not to exceed 90 days.

Revocation of License

In case a physician or surgeon shall be convicted of violating any of the provisions of section 147.11, the State Board of Medical Examiners, upon a first conviction, may, and, upon a second conviction, shall revoke the license of the person so convicted, but such revocation shall be subject to the right of the person whose license has been so revoked to appeal to the district court of the proper county on questions of law and fact.

Minnesota Statutes 147.11, 147.12, 147.13.

Captain Cook's Spruce Beer for Scurvy

At the turn of the century, Captain Cook provided his crew with sauerkraut, and encouraged them to seek wild vegetables whenever he landed to preserve their health during a four-year voyage in his ship Discovery. He also provided them with spruce beer, which was considered to be agreeable and wholesome, suggesting that this be drunk instead of rum, despite the fact that the sailors did not relish the change.

The beer was made as follows:

Boil down to concentration young black spruce fir branches — ½ pt.

Add bruised pimento — 4 ounces, ginger — 4 ounces, and water — 3 gallons.

Boil for 5 or 10 minutes, strain, and add 11 gallons of warm water, 1 pint of yeast, and 6 pints of molasses.

Mix and allow the mixture to ferment for 24 hours. Drink abundantly.

—The Practical Family Physician, Hood Medical Book Company, 1901

Comparative Incidence of Mycotic Diseases Involving the Adrenal Gland[‡]

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THIS STUDY was undertaken in an attempt to ascertain the incidence, type, and degree of involvement of the adrenal glands in patients who have various mycotic infections.

Materials and Methods

Sixty-two cases of systemic mycotic infections in which necropsy had been carried out at the Mayo Clinic during the period 1917 through October 1, 1960, form the basis of this report. The case records and necropsy protocols were reviewed. The gross adrenal specimens available were re-examined, and additional microscopic sections were made of them and stained. The histochemical stains employed included hematoxylin and eosin, azure eosin (pH 4.5), silver chromate, Gram, periodic acid-Schiff, and the acid-fast. The elastic van Gieson and Mallory-Heidenhain stains were applied later to delineate vascular involvement.

Criteria used to verify the diagnosis of a fungal infection included the results of antemortem and post-mortem cultures, when available, and histologic identification of the organism in the adrenal glands as well as in other organs.

Anatomic destruction of the adrenal cortex was graded on a 0 to 4 basis on examination of both gross specimens and microscopic sections. Grade 0 signified essentially intact adrenal glands; small, infrequently-occurring granulomatous foci of organisms were included in this grade. Grade 1 destruction was employed when at least 10 per cent of the adrenal tissue was intact, grade 2 when approximately 5 to 10 per cent remained intact, grade 3 when 5 per cent or less remained intact, and grade 4 when no intact adrenal cortical tissue could be demonstrated.

Results

The fatal granulomatous infections in the 62 cases are listed in the Table. The adrenal glands were involved by the mycotic process in 13 of the 62 patients (21 per cent). Of

TABLE
Distribution of Cases According to Mycotic Disease and Incidence of Adrenal Involvement

Mycotic disease	Number	Number with adrenal involvement	Incidence, per cent
Actinomycosis or nocardiosis	33	2	6
Cryptococcosis	9	3	33
Histoplasmosis	8	8	100
Aspergillosis	7	0	0
Blastomycosis	2	0	0
Coccidioidomycosis	2	0	0
Sporotrichosis	1	0	0
Total	62	13	21

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‡See Dec. 1964 issue of Minnesota Med., page 1460.

these 13 patients, eight had histoplasmosis, three had cryptococcosis, and two had either actinomycosis or nocardiosis, but the specific genus of the last two was not determined by the cultures made.

There were no massive destructive lesions of the pituitary glands or gonads in any of the 13 cases.

Of the 13 patients who had involvement of the adrenals, 10 were males and three were females. Ages ranged from seven months to 77 years.

Whether clinical adrenal insufficiency was present in these 13 cases was difficult to determine for several reasons: (1) In some cases, adrenal involvement was not suspected ante mortem and hence diagnostic procedures for this condition were not employed. (2) In certain cases, biochemical criteria were not available at the time the patient underwent clinical examination, even if the diagnosis was suspected. (3) In cases in which more than the one disease was present, the symptoms were difficult to analyze in retrospect, and it was not easy to distinguish the symptoms that were attributable to the specific disease.

Cryptococcosis (Fig. 1)

The adrenal involvement apparently is a more or less terminal event in this disease. The duration of the disease was longer in our patients with adrenal involvement than in those without such involvement. In patients with adrenal involvement, the disease was disseminated, while patients without adrenal involvement had more localized disease. Although three of our nine patients with cryptococcosis had adrenal involvement of grade 1, none presented evidence of adrenal insufficiency. However, adrenal failure due to cryptococcosis has been reported in the literature.[1]

The association of cryptococcosis with other diseases, especially lymphoma and leukemia, has been emphasized in the literature.[2-5] Hodgkin's disease was associated in one of our three cases in which the adrenals were involved. In two of these three cases, no ante-mortem or post-mortem cultures were available. However, in these two, typical Cryptococcus neoformans could be demonstrated histopathologically both in the adrenal glands and in the brain. In the third, positive cultures were obtained both before and after death.

Actinomycosis and Nocardiosis

Fungi in the family of Actinomycetaceae are indistinguishable morphologically (Fig. 2) in tissue sections and can be differentiated only with certainty by cultural technics.

Although cases of actinomycosis or nocardiosis comprised the largest group in our series, the adrenal glands were involved in only two of them. Organisms consistent morphologically with either species of Actinomyces or Nocardia were seen in the adrenals

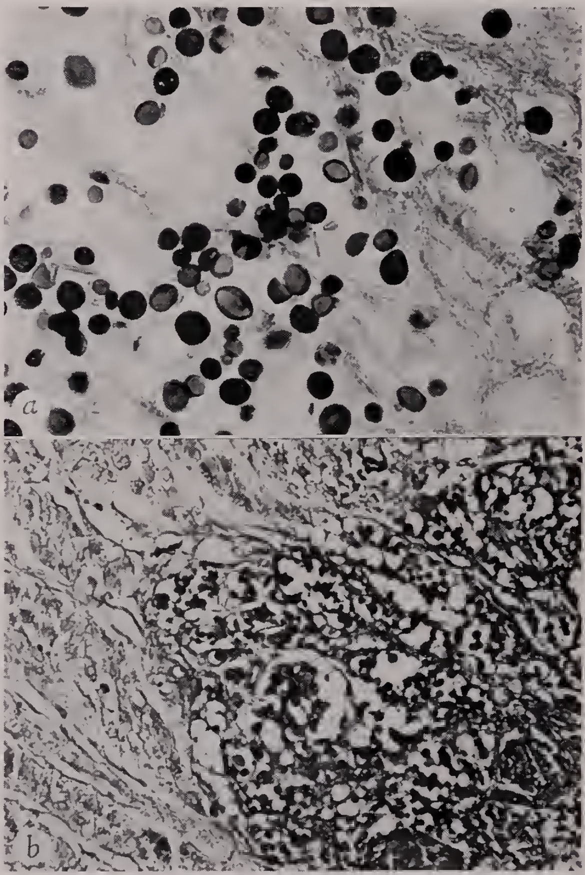

Fig. 1.*(a)* — Cryptococcus neoformans stains black in the center with silver chromate, whereas the capsule appears as a clear halo. Note budding in right upper corner of the field (silver chromate; x800). *(b)* Cortex of right adrenal gland of patient with disseminated cryptococcosis. The lesion is composed of yeastlike cells. A typical area is seen in right lower field. Grade of destruction is 0 (silver chromate; x200).

in both cases, and, in both, the adrenal involvement tended to be mild (grade 1) and unilateral. Direct extension was suggested by the finding of renal infection on the side affected; the opposite kidney was free of mycotic lesions. The disease in these two cases was more chronic than in the cases of either cryptococcosis or histoplasmosis in which the adrenal glands were involved. In one case, the process lasted two and a half years. The duration of the disease tended to be longer in the patients with adrenal involvement than in patients who had disseminated actinomycosis or nocardiosis. As was true of cryptococcosis, adrenal involvement seemed to be only a terminal event and a function of chronicity in these two cases. In both cases, there was no evidence of adrenal insufficiency. Although nocardiosis has been reported with adrenal involvement, as far as could be ascertained from the literature there has been no recorded case of actinomycosis that involved the adrenal glands.

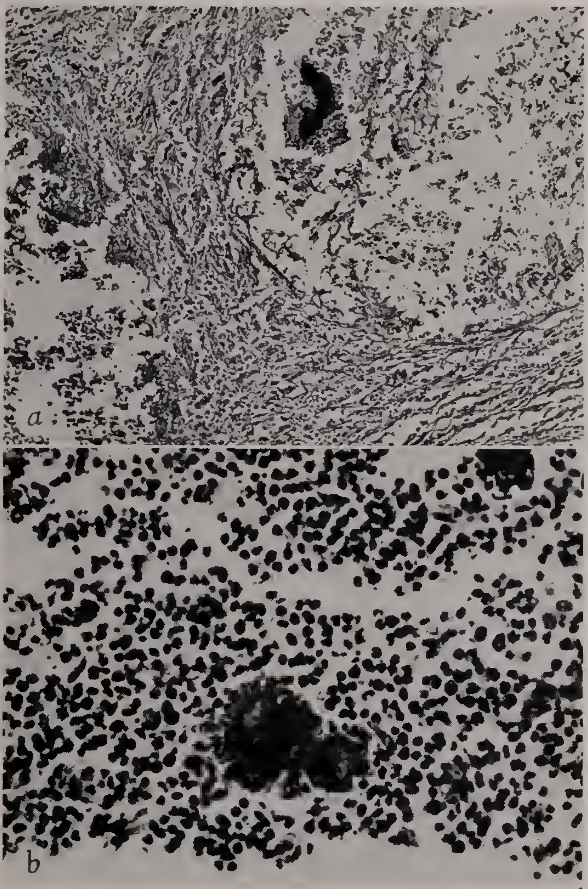

Fig. 2.(a) — Cortex of right gland of patient with findings compatible with actinomycosis or nocardiosis. The organism stains dark with silver chromate. Intact cortex is seen between the two abscesses. Grade 1 destruction (silver chromate; x100). *(b)* Cortex of left adrenal gland of same patient showing fungi. The central portion of ray fungus is gram positive. Grade 1 destruction (Gram; x400).

Histoplasmosis

Adrenal involvement was present in all eight cases of histoplasmosis; in four, destruction was graded 1 and in the remaining four, it was graded 3 or 4. The adrenal involvement was bilateral in five of the eight cases. The diagnosis was confirmed in all cases by both culture and identification of the organism in the adrenal gland, and the disease was disseminated throughout the body.

In four of the eight cases there was evidence of thrombosis in the central adrenal vein, which was bilateral in one case. This finding will be elaborated on in a separate report. Three of the four patients with suggestive evidence of clinical adrenal failure and the one patient with probable insufficiency demonstrated the vascular lesion.

Treatment

The patients who had cryptococcosis, actinomycosis, or nocardiosis were not treated with cortisone or allied agents. Four of the eight patients who had histoplasmosis with involvement of the adrenal glands had antemortem symptoms that suggested adrenal insufficiency, and one patient had probable insufficiency based on laboratory evidence. In these five cases, treatment with cortisone or allied agents was attempted, but the widespread disease and terminal status of the patient made recovery unlikely.

Comment

Our results with regard to cryptococcosis and nocardiosis or actinomycosis do not differ essentially from those of other investigators in regard to the incidence and the mildness of adrenal involvement and the rarity of Addison's disease due to such pathogens. Nocardia involves the adrenal glands only rarely and to our knowledge no reports that describe actinomycosis with such involvement have appeared in the literature.

The adrenal glands were involved in all eight of our cases of histoplasmosis; this was the highest incidence of adrenal involvement by a pathogen in our 62 cases. Review of the recent literature also indicates that histoplasmosis is the commonest mycotic process to involve these glands.[1,6]

Prior to 1934, only seven cases of histoplasmosis had been described in the literature.[7,8] One of the latest reviews of disseminated histoplasmosis was concerned with 25 cases. Nineteen of the 25 patients died; a necropsy study of 17 indicated that 14 had adrenal involvement.[9] The vascular changes found in adrenal glands involved by Histoplasma capsulatum may represent a hitherto unrecognized aspect of this disease. Sudden decline in the clinical status of a patient who has histoplasmosis may alert one to the possibility of hemorrhagic infarction of the adrenal gland.

Our findings corroborate the contentions that adrenal involvement is prominent in cases of generalized histoplasmosis, that such involvement is usually marked, and that the clinical picture of adrenal insufficiency is common.

The adrenal glands were not involved by the mycotic process in any of the cases with aspergillosis, coccidioidomycosis, blastomycosis, or sporotrichosis, but other investigators have described such involvement by Blastomyces dermatitidis and Coccidioides immitis. In one series of 347 cases of blastomycosis, adrenal involvement was present in two.[4,10] In another series of 90 cases of blastomycosis, the adrenals were involved in two.[11] Tuttle and Lichtwardt,[12] in 1953, reported a case of disseminated blastomycosis with adrenal involvement in which the organism simulated Histoplasma capsulatum. Forbus and Bestebreurtje,[13] in a review of 95 cases of disseminated coccidioidomycosis, found adrenal involvement in 16 cases; but in no case was there evidence of adrenal failure.

Summary

The adrenals were involved by the mycotic process in 13 of the 62 cases of mycotic infections that came to necropsy at this clinic from 1917 through October 1, 1960, giving a total incidence of approximately 21 per cent. The diagnosis in eight of these 13 cases was histoplasmosis, in three, cryptococcosis and in two, either actinomycosis or nocardiosis.

The adrenals were involved in all cases of histoplasmosis, and our results corroborate the contention that histoplasmosis is the fatal mycotic process that most consistently involves the adrenals. In five of the eight cases of histoplasmosis, death appeared to be secondary to adrenal insufficiency.

The adrenal glands were involved by the mycotic process in three of the nine cases of cryptococcosis, but symptoms were not suggestive of adrenal failure in any of these cases.

Thirty-three of the 62 patients had either actinomycosis or nocardiosis, but since only two had adrenal involvement without clinical findings suggestive of adrenal insufficiency, our results corroborate those in the literature that indicate the mild degree of adrenal involvement and the rarity of Addison's disease in these infections.

Of the 62 patients, seven had aspergillosis, two had blastomycosis, two had coccidioidomycosis, and one had sporotrichosis. None of the seven patients with aspergillosis had involvement of the adrenal glands by the mycotic process, although other investigators have described such involvement by blastomycosis and coccidioidomycosis.

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Rice County Society Donates to Scholarship Fund

The Scholarship and Loan Fund of the Southern Minnesota Medical Association has now been in operation since 1958. Loans have been made to 25 students at the University of Minnesota Medical School. The loan fund has been made possible by donations from various medical societies in southern Minnesota and the Southern Minnesota Medical Association itself. Since its beginning the following medical societies have made donations: Wabasha Medical Society, Winona Medical Society, Blue Earth Valley Medical Society, Rice County Medical Society, Renville-Redwood County Medical Society, Steele County Medical Society, Zumbro Valley Medical Society, Blue Earth County Medical Society, Brown County Medical Society, and McCleod County Medical Society. This loan fund through the generosity of medical societies and doctors of southern Minnesota has grown to the sum of $11,614.10. Anticipating continued need for such funds has led the Rice County Medical Society to begin this year's contributions with a check for $500.

This Loan Fund is available to all students at the University of Minnesota Medical School without interest during their academic and internship periods. A small rate of interest is charged after the completion of their internship. One of the main purposes of this Loan Fund, in addition to helping the students, is to interest the students in going into the general practice of medicine particularly in the state of Minnesota.

There are people who fail because they are afraid to make a beginning; who go to bed tired because they spend the day looking for an easy job; who cannot tell what they think about anything until they see what the morning paper has to say about it.
—George Rinliff in The Uplift

As people get better off, they sometimes have too much to live on and too little to live for.—Herbert Prochnow

He who suffers, remembers.—Cicero

Solid Cell Carcinoma

of
the
Thyroid

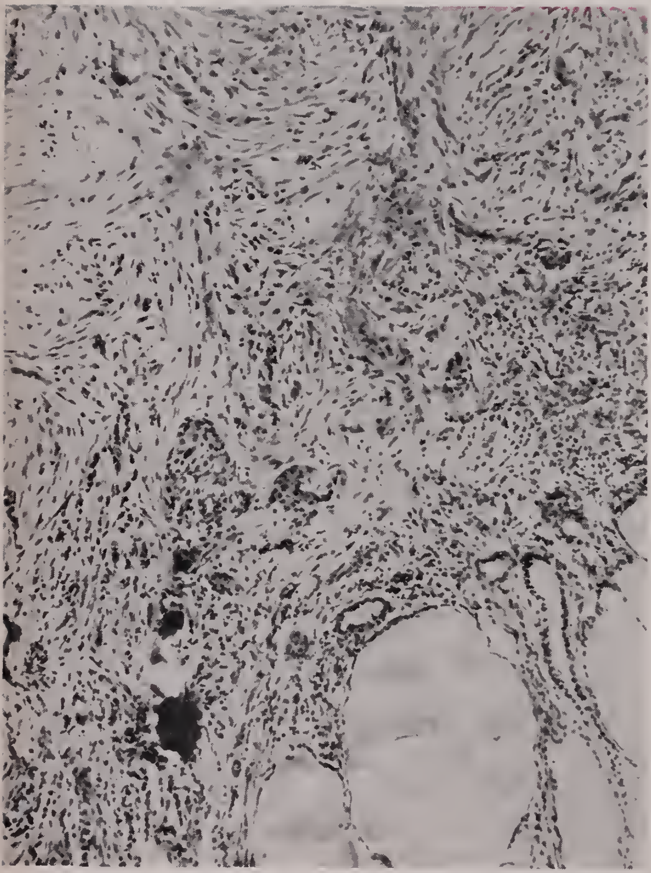

Fig. 1 — Solid Cell Carcinoma of Thyroid (H & E; x 250). Normal Acini Lower Right, Sheets of Tumor Cells with Fibrous "Amyloid" Stroma Above.

SOLID CELL carcinoma of the thyroid with amyloid stroma is an infrequently encountered malignancy of the thyroid gland, and its true significance has until recently been obscure. Our interest in this entity was stimulated by a patient who presented with just such a pathological picture.

Case Report

A 48-year-old male noted a mass in the right side of the neck in April, 1964. He consulted his local physician who removed a portion of the mass and submitted it for pathological examination. The microscopic appearance was felt to be characteristic of solid cell carcinoma of the thyroid with amyloid stroma. The patient was subsequently referred to this clinic for further evaluation and treatment. On examination the mass seemed to be lodged behind the sternoclavicular insertion of the right sternocleidomastoid muscle and fixed to the deep tissues. It appeared to be firm and rubbery. The thyroid gland proper was not enlarged. Multiple small nodes were palpable within the area of the anterior triangle of the right neck. The patient was clinically and chemically euthyroid and the tumor did not take up I^{131}. There was no evidence of direct invasion of the clavical or distant bone metastasis by X-ray examination.

At operation the entire thyroid gland had a normal appearance and consistency. A total right lobectomy, including the pyramidal lobe and isthmus, was car-

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with Amyloid Stroma

ried out. The mass underlying the sternocleidomastoid muscle was removed in continuity with a radical right neck dissection. The cervical lymph nodes of the internal jugular chain up to the level of the jugular foramen were obviously involved with metastatic implants. The immediate postoperative course was complicated by diffuse bleeding from the operative area, requiring surgical control. Subsequently, however, the patient made an uncomplicated recovery and was discharged in early June of 1964.

Discussion

Medullary or solid carcinoma of the thyroid with amyloid stroma was first recognized as a distinct clinicopathologic entity by Hazard, Hawk and Crile[1] in 1959. As early as 1910, however, Stoffel[2] had noted the presence of unusual amyloid deposits in several specimens of thyroid carcinoma, and had speculated as to their origin and significance. Again, in 1951, Horn[3] presented seven cases of thyroid malignancy of an unusual type, some of which possessed many of the clinical and morphological characteristics of solid carcinoma. He did not, however, subject his material to stains for amyloid. It remained therefore for Hazard et al. to recognize and to focus attention on the true significance of this uncommon but important variant of thyroid carcinoma.

Solid Cell Carcinoma of Thyroid

Carcinomas of the solid cell type possess several distinctive morphological features. They are usually composed of moderate sized, round to oval shaped epithelial cells arranged in broad sheets, with little evidence of organization and with virtually complete absence of colloid production or papillary formation. This is in sharp contrast to other thyroid neoplasms, of which about 66% are mixed types. However, considerable variability in cellular morphology may be present; at times the tumor may closely resemble neurogenic sarcoma, transitional cell carcinoma, islet cell tumor of the pancreas or carcinoid.[1,4]

Interspersed among these clumps of cells are bands of connective tissue and an amorphous hyaline material which yields a yellow-green fluorescence when stained for amyloid. It is this material which provides the tumor with its most distinctive features. While some observers have noted periodic acid Schiff stain positive material in the normal juxtaneoplastic acini,[5] the amyloid is primarily intraneoplastic and intercellular in location. It is regularly found in the primary focus and in metastases as well. In addition, Russell et al.[4] have noted that the kidneys of seven of ten patients with solid cell carcinoma demonstrated tubular changes characteristic of plasma cell myeloma, and they infer from this that the tumor produces some as yet unidentified protein which is excreted via the kidney, exciting these tubular changes in transit. Vassar[5] has further elaborated on this hypothesis. He noted that Spicer[6] demonstrated an increased sialic acid component in thyroglobulin glycoprotein obtained from rats with experimentally induced thyroid carcinoma, and suggests that periodic acid Schiff stain positive material actually represents altered thyroglobulin produced by the tumor cells, indicating a certain degree of differentiation and functional activity. Further investigation on this subject is in progress.

Incidence

Review of the literature reveals 104 documented cases of solid carcinoma of the thyroid,[1,4,5,7,8,9] which appears to comprise from 3 to 10% of all thyroid malignancies. It is usually encountered in the sixth or seventh decade of life and is seen twice as frequently in women as in men. The presenting complaint is often goiter of long duration, frequently associated with enlarged cervical lymph nodes. One reported case[9] came to definitive surgery after a cervical node present for seven years proved to harbor solid cell carcinoma at biopsy. Woolner et al.[9] have documented four cases in which this tumor was probably present from 10 to 30 years at least. While there does not appear to be any favored location for the primary focus, a striking feature of this neoplasm is its tendency to spread to regional lymph nodes relatively early in the course of the disease. Hazard found 58% regional node involvement at the time of surgery, while Woolner noted 59.5% and Hirabayashi[8] 91%. Accordingly, a relatively high proportion of patients in this group undergo radical neck dissection. Distant metastases are not uncommon late in the disease, having a predilection for lung, liver and bone.[9]

Surgical Treatment

In general, the surgical treatment of solid carcinoma has been far from uniform, the majority of patients undergoing total or subtotal lobectomy. One of the most telling arguments in favor of utilizing radical subtotal or total thyroidectomy to treat the more common thyroid carcinomas is the fact that most appear to be multicentric in origin.[10-13] Russell et al. performed subserial sections on 80 glands removed for carcinoma and found that in 87.5% of them foci of tumor could be demonstrated in the isthmus or contralateral lobe. Most of this material, however, was of the papillary or mixed variety. Nevertheless, Woolner et al. found both lobes involved in 10% of their cases of solid carcinoma, while Hirabayashi noted a 41% incidence of bilaterality on routine serial sections. The actual number of glands containing solid carcinoma bilaterally may well be higher, since Russell found evidence of multicentricity in only 30% of his cases when sectioned in this routine manner.

Prognosis

Statistics indicate that solid carcinoma falls somewhat between the papillary and anaplastic varieties with regard to five-year survivorship. Woolner found a 75.6% five-year and 61.3% ten-year survival rate, which is in substantial agreement with other series. Hirabayashi compared solid carcinomas with follicular carcinoma of the invasive type and found a 20-year survivorship of 32.1% for the former, as opposed to 7.8% survivorship for the latter. The majority of deaths occurred from extensive local recurrences following surgery.

Summary

Solid carcinoma of the thyroid is a relatively uncommon neoplasm characterized by slow growth, early affinity for regional nodes, amyloid deposition in the tumor parenchyma, absence of "mixed" tumor elements, and long survivorship following adequate surgical extirpation.

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Leo Rosten's Creed

We must forever oppose hysteria, even when it is wrapped in the vestment of patriotism.

We must learn that those we like are not always right, and those we don't like are not always wrong.

We must learn to seek change without violence.

We must try to understand each other by reconciling ourselves to the fact that most of us never really mature; we simply grow taller.

We must meet fanaticism with courage and idealism with a dose of caution.

We must be skeptical of that which is promised but not proved.

We must be strong enough to be gentle.

We must know that life will always contain unbearable stretches of loneliness.

We must have the great good courage to live without absolutes, without dogmas.

We must have the will to seek imaginative escape from conformity.

Vision

Don't worry too much about what lies ahead. Go as far as you can see, and when you get there, you can see farther on.—Great West Life Bulletin

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Genius is the power of making continuous efforts.—Source unknown

Smoking Habits and Disease

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A HIGH degree of relationship between cigarette smoking and death rates of men has been found in six previous prospective studies carried out in this country, Great Britain, and Canada.[1-6] In this paper, we will present findings on this subject in the first 35.5 months of follow-up in the Minnesota segment of a large prospective epidemiological study which was started in 1959 and is still in progress.[7-10]

Method of Study

During the latter part of 1959 and early 1960, volunteer workers of the Minnesota Division of the American Cancer Society enrolled 74,620 men and women, the mean date of enrollment being October 18, 1959. The study area encompasses 56 of the 87 counties of Minnesota. Upon enrollment, each subject answered a detailed questionnaire covering many factors including past and present smoking habits. The subjects are traced once a year and are requested to fill out brief questionnaires once every two years. In the most recent completed follow-up, 99.96% of the subjects were traced through September 30, 1962. (The next follow-up was started on October 1, 1963, and is still in progress.) When a death is reported, we request the Minnesota Health Department to supply us with a copy of the death certificate; and when cancer is mentioned on a death certificate we request the doctor to supply additional information.

This report is confined to the records of 31,733 men between the ages of 40 and 89 who were traced through September 30, 1962. Of these 31,733 men, 1,459 (4.6%) were reported to have died; and we now have copies of the death certificates on 1,455 of them. Cancer was mentioned on 262 of the certificates and doctors have provided additional information on 89% of them.

Physical Complaints

A list of various physical complaints was printed on the first questionnaire and the subject was asked to check "yes" or "no" after each of them to indicate whether or not he had the complaint "at present." Those who had a complaint were asked whether it was "slight," "moderate" or "severe." Of the 31,733 men between the ages of 40 and 89, 8,250 said that they were currently smoking 20 or more cigarettes a day and 8,403 said that they had never smoked regularly. Table 1 shows the number and percent of these smokers who reported having various complaints and the percent of non-

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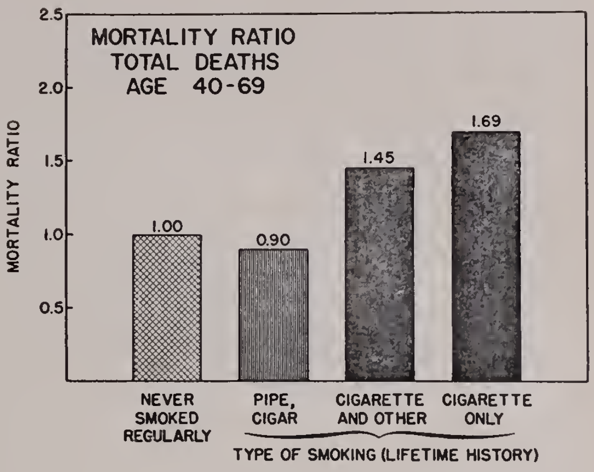
*Minnesota Division of the American Cancer Society and the Statistical Research Section of the Medical Affairs Department of the American Cancer Society, Inc.

in Minnesota*



smokers who reported having the complaints. The percentages for the nonsmokers have been adjusted to the age distribution of the cigarette smokers (this being necessary for comparability since the nonsmokers tended to be older than the cigarette smokers).

Pulmonary Symptoms

Cough, shortness of breath, and pain or discomfort in the chest were all reported far more frequently by the cigarette smokers than by the nonsmokers, the ratio being 2.98 to 1 for cough, 1.97 to 1 for shortness of breath and 1.38 to 1 for pain or discomfort in chest. Considering only subjects who reported these complaints to a moderate or severe degree, the ratios were 4.29 to 1 for cough, 2.52 to 1 for shortness of breath and 1.55 to 1 for pain or discomfort in chest. These findings are consistent with findings in histologic studies of changes in lung tissue in relation to cigarette smoking.[11,12] Such studies have shown a high degree of association between cigarette smoking and: (1) hyperplasia and the occurrence of cells with atypical nuclei in bronchial epithelium, (2) hyperactive glands in the walls of bronchial tubes, and (3) changes in the lung parenchyma including rupturing of alveolar septums, fibrosis and thickening of the walls of arterioles and small arteries.

Gastrointestinal Symptoms

Loss of appetite was reported over three times as frequently by cigarette smokers as by nonsmokers. One might expect this to be associated with loss of weight; and loss of weight during the preceding two years was reported somewhat more frequently by cigarette smokers than by nonsmokers. However, gain of weight was also reported somewhat more frequently by cigarette smokers than by nonsmokers. This suggests that fluctuations in weight may occur somewhat more frequently in cigarette smokers than in nonsmokers.

A number of other physical complaints such as hoarseness, nausea or vomiting, pain in stomach, indigestion, diarrhea and a tendency to "fatigue easily" were also reported somewhat more frequently by cigarette smokers than by nonsmokers. The picture in general indicates that cigarette smokers, as a group, tend to feel less physically fit than do nonsmokers.

Mortality

Table 2 shows the men classified by type of smoking (lifetime history). The figures under the heading "observed" are the actual number of deaths reported from the start of the study through September 30, 1962.

Nonsmokers

Figures under the heading "expected" are the number of deaths which would have occurred if the age-specific death rates in each group had been the same as the age-specific death rates of men who never smoked regularly. In other words, the age-specific death rate of the nonsmokers is taken as a standard for comparison. The mortality ratio is the observed number of deaths divided by the expected number of deaths. By definition, the mortality ratio of the nonsmokers is 1.00.

Cigarette Smokers

Men with a history of only cigarette smoking had by far the highest death rates (as indicated by their high mortality ratios). In age group 40 to 69, the death rate of such cigarette smokers was 69% higher than the death rate of nonsmokers; and in age group 70 to 89 the death rate of such cigarette smokers was 36% higher than the death rate of nonsmokers. (See Figure 1).

Cigarette, Pipe and Cigar Smokers

The death rate of men who smoked cigarettes and also smoked pipes or cigars (i.e., the "cigarette and other" group) was somewhat lower than the death rate of men who smoked cigarettes only. This is accounted for by the fact that men with mixed smoking habits tend to smoke fewer cigarettes per day and tend to inhale the smoke less deeply than do men who smoke only cigarettes.

Pipe and Cigar Smokers

The death rate of pipe and cigar smokers was close to the death rate of nonsmokers. This appears to be due to the fact that the great majority of pipe and cigar smokers do not inhale the smoke or inhale it only to a slight degree.

Table 3 shows further details on current cigarette smokers (i.e. men who were smoking cigarettes regularly at the time they enrolled in the study) with a history of only cigarette smoking. It is confined to men between the ages of 40 and 69 for the reason that there were relatively few such cigarette smokers among men in the older age groups. Some of the figures (particularly mortality ratios) are rather unstable statistically, due to small numbers. Figures for nonsmokers are included to give a basis for comparison.

Heavy Smokers

The mortality ratio increased substantially with the number of cigarettes smoked per day and was substantially higher among cigarette smokers who said that they inhaled the smoke deeply than among those who said that they did not inhale the smoke. The cigarette smokers who took up the habit before they reached their 20th birthday had higher death rates than did cigarette smokers who started the habit later in life.

Coronary Disease

Death certificates indicated that coronary artery disease accounted for 679 (46.5%) of the 1,459 deaths. Deaths from this cause were highly associated with the smoking habits of men in age group 40 to 69 but less highly associated with the smoking habits of men in age group 70 to 89. In age group 40 to 69, the coronary artery disease mortality ratios were: 1.00 for men who never smoked, 1.03 for pipe and cigar smokers, 1.75 for men who smoked cigarettes and also smoked pipes or cigars and 1.90 for men who smoked only cigarettes. The corresponding mortality ratios for men in age group 70 to 89 were 1.00, 0.98, 1.23 and 1.20 respectively.

Lung Cancer

Lung cancer accounted for 37 deaths (31 in age group 40 to 69 and 6 in age group 70 to 89). Four of these 37 men said that they had never smoked regularly and all of the others had a history of cigarette smoking.

Other Cancers

Previous studies have shown a relationship between smoking habits and the occurrence of cancer of the buccal cavity, pharynx, larynx, esophagus and bladder. Of 24 men who died of cancer of these sites, three said that they never smoked regularly, four were pipe and cigar smokers (who never smoked

TABLE 1

Physical complaints reported by 8,250 men who smoked 20 or more cigarettes per day and by 8,403 men who never smoked regularly. Age group 40 to 89.

Physical Complaint	Cigarette Smokers with Complaint No. of Men (a)	Cigarette Smokers with Complaint % (b)	Nonsmokers with Complaint % (c)	Ratio (b)÷(c) (d)
Cough (slight, moderate, severe)	4,802	58.2	19.5	2.98
Cough (moderate or severe)	2,332	28.3	6.6	4.29
Shortness of breath (slight, moderate or severe)	3,057	37.1	18.8	1.97
Shortness of breath (moderate or severe)	1,267	15.4	6.1	2.52
Pain or discomfort in chest (slight, moderate or severe)	1,452	17.6	12.8	1.38
Pain or discomfort in chest (moderate or severe)	488	5.9	3.8	1.55
Loss of appetite	599	7.3	2.7	2.70
Loss of weight	608	7.4	5.3	1.40
Gain of weight	342	4.1	3.0	1.37
Hoarseness	998	12.1	10.1	1.20
Nausea or vomiting	449	5.4	3.9	1.38
Indigestion	1,893	22.9	18.2	1.26
Pain in stomach	1,316	16.0	12.3	1.30
Diarrhea	597	7.2	5.5	1.31
Fatigue easily	2,928	35.5	25.6	1.39

TABLE 2

Mortality by type of smoking (lifetime history)

Type of Smoking (Lifetime History)	Age 40-69 No. of Men	Age 40-69 No. of Deaths Obs.	Age 40-69 No. of Deaths Exp.	Age 40-69 Mortality Ratio	Age 70-89 No. of Men	Age 70-89 No. of Deaths Obs.	Age 70-89 No. of Deaths Exp.	Age 70-89 Mortality Ratio
Never Smoked Regularly	7,431	213	213.0	1.00	1,221	187	187.0	1.00
Pipe, Cigar Only	2,131	66	73.0	0.90	709	114	110.6	1.03
Cigarette and Other	5,999	224	154.8	1.45	490	84	68.7	1.22
Cigarette Only	13,251	478	282.8	1.69	501	93	68.3	1.36
Total	28,812	981	723.6	1.36	2,921	478	434.6	1.10

TABLE 3

Mortality by amount of cigarette smoking, degree of inhalation and age began cigarette smoking. Age group 40 to 69.

Current Cigarette Smoking	No. of Men	No. of Deaths Obs.	No. of Deaths Exp.	Mortality Ratio
Cigarettes per day:				
1 to 9	1,233	50	31.6	1.58
10 to 19	2,113	84	47.1	1.78
20 to 39	5,443	182	101.6	1.79
40+	841	29	13.1	2.21
Degree of Inhalation:				
None	729	17	19.5	0.87
Slight	1,451	68	35.8	1.90
Moderate	5,444	187	103.6	1.81
Deep	1,987	73	33.9	2.15
Age Began Cigarette Smoking:				
25+	996	31	25.8	1.20
20 to 24	2,610	87	52.9	1.64
15 to 19	4,961	180	92.7	1.94
< 15	797	32	15.7	2.04
Never Smoked Regularly	7,431	213	213.0	1.00

cigarettes), and 17 had a history of cigarette smoking.

Emphysema

Twenty men died of emphysema and all of them were smokers. Two smoked only pipes or cigars, seven smoked cigarettes and also smoked pipes or cigars and 11 smoked only cigarettes.

Hospitalization

At the time of the second follow-up (approximately two years after the start of the study) surviving subjects were requested to fill out a second questionnaire. On this questionnaire, they were asked whether or not they had been hospitalized since October 1, 1959 (the date the study was started). Of course, nonsurvivors did not fill out these questionnaires; but we assumed that all those who died had been hospitalized prior to death, this being true in the great majority of cases.

In Table 4, men aged 40 to 69 are classified in groups by their smoking habits as reported on the first questionnaire; and the percent hospitalized is shown for each of these groups. For comparability, the percentages have been standardized for age on the basis of the age distribution of all the men in the study.

TABLE 4

Percent of men hospitalized between start of study and second follow-up (approximately 2 years). Men aged 40 to 69 at start of study. Percentages are standardized for age on the total population of enrollees in the state.

Smoking Habits	Percent Hospitalized
Never Smoked Regularly	14.8
Cigar, Pipe	16.4
Cigarette and Other	20.2
Cigarette Only	19.6
Current Cigarette*	19.6
1-9 a day	16.0
10-19 a day	19.1
20-39 a day	20.1
40+ a day	24.7
Do Not Inhale	15.1
Inhale Slightly	18.5
Inhale Moderately	19.4
Inhale Deeply	23.9
Age Began Smoking:	
25 or older	15.9
20 to 24	18.2
15 to 19	20.7
Before age 15	23.7

*Men with a history of only cigarette smoking who were currently smoking cigarettes at the time of enrollment.

The general picture is much the same as that previously shown for total mortality. Only 14.8% of the men who never smoked were hospitalized within two years, while 19.6% of the men with a history of only cigarette smoking were hospitalized during the same period of time. Among current cigarette smokers, the risk of hospitalization increased with amount of smoking from 16.0% for those who smoked 1 to 9 cigarettes per day to 24.7% for those who smoked 40 or more cigarettes per day. The percent of men hospitalized was greater among cigarette smokers who said that they inhaled deeply than among those who said that they did not inhale; and it was greater among men who started to smoke cigarettes early in life than among those who started to smoke later in life.

Summary and Discussion

In this paper, we have reported on the smoking habits in relation to the physical complaints of 31,733 Minnesota men aged 40 to 89; and have reported the mortality and hospitalization experience of this group of men during the first 35.5 months after they were enrolled as subjects in a prospective epidemiological study. The findings are in good agreement with findings previously reported from other epidemiological studies on this subject.

Cigarette smokers report physical complaints (particularly cough, shortness of breath and loss of appetite) more frequently than nonsmokers, are hospitalized more frequently than nonsmokers, and have far higher death rates than nonsmokers. Among cigarette smokers, the frequency of physical complaints, the frequency of hospitalization and the death rate increase with amount of cigarette smoking, increase with degree of inhalation of the smoke and are higher among cigarette smokers who started to smoke early in life than among those who started to smoke late in life.

As in past studies, death rates from lung cancer, cancer of certain other sites, emphysema and coronary artery disease were found to be higher in cigarette smokers than in nonsmokers.

There is no need for us to review the literature and discuss other evidence on the subject of smoking and health since this has been done many times before. We conclude that cigarette smoking constitutes a major health hazard in Minnesota as well as in other parts of the world.

Acknowledgements

We would like to thank the 31,733 men who volunteered as subjects for this study; the volunteer workers of the Minnesota Division of the American Cancer Society who enrolled and traced the subjects; the Minnesota Department of Health that provided us with copies of death certificates; and the many physicians who provided us with additional medical information on subjects who died of cancer.

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I owe a greater obedience to God than to you, gentlemen. So long as I draw breath I shall never stop elucidating the truth before everyone I meet, asking "Are you not ashamed to pursue money and give no thought to truth and understanding and the perfection of your soul?" I shall not alter my conduct even if I must die a hundred deaths, for God has appointed me to act the gadfly. Death does not matter. What matters is that I should do no wrong.—Socrates

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Some men carry their ego all over the place.—C.O.R.

Each generation creates its own devils, and meets its own Waterloo on the heartless field of reality. The Christian Fathers blamed the Prince of Darkness for preventing perfectable man from reaching Paradise. Anarchists blamed the state. Marxists blamed the class system. Pacifists blamed the militarists. Our latter day intellectuals seem to blame the mass media for their lamentable failure of more people to obtain the bliss of intellectual grace.—Leo Rosten

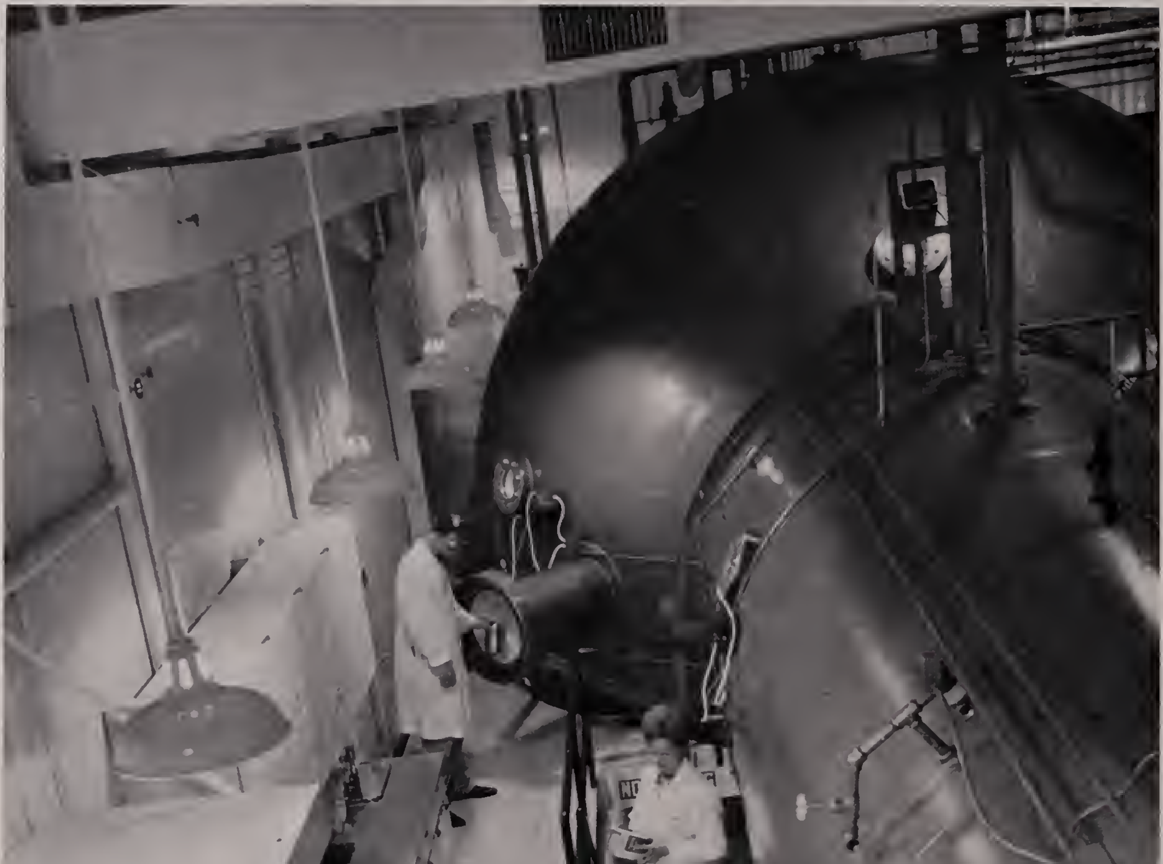

Fig. 1 — Hyperbaric Medical Facility.

Hyperbaric Medical Facility*

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DURING RECENT months a complex hyperbaric research facility has been opened at the Hennepin County General Hospital. Designed as four chambers, this unit is the culmination of two and one-half years of engineering and construction. During the first six months of operation the chambers were used for 188 treatment cycles at a pressure of three atmospheres absolute (the pressure equal to 66 feet of depth in sea water). Many unique features of design and function have been incorporated in this unit and will be described.

Although attempts to apply conditions of high pressure environment to medicine have appeared sporadically over the years, not until our time has medical and surgical practice been well poised to pursue this method.[1] Early in our engineering of this facility we were impressed with the dangers inherent in the application of high pressures to human subjects. The need for maximum safety of both design and operation of hyperbaric chambers was paramount in our thoughts. In addition, the value of a unit containing multiple chambers permitting wide flexibility of operation on a clinical basis was appreciated. We believe our chambers are well suited to both basic and applied clinical research on a broad scale.[2]

Engineering, installation, and fitting out of the chambers were completed by the Vacudyne Corporation, Chicago Heights, Illinois. The Chicago Bridge and Iron Co., Chicago, Illinois, fabricated, erected and tested the steel vessels. The systems for high pressure reserve air and medical gases were engineered by the Air Products Corporation, Allentown, Pennsylvania; The Oxequip Co., Chicago, Illinois, designed, constructed and installed the control systems for medical gases, differential suction, and reserve air.

Historical Review

Robert Boyle, the English physicist, in 1659 was the first to show that a "vital material" in the air (oxygen) was necessary for maintaining life. His experiments demonstrated bubbles of gases which appeared in the tissues of animals if they died under conditions of decreased (hypobaric) ambient pressure. The first practical application of hyperbaric conditions, however, was made by Triger, a Frenchman, who in 1841 developed the first caisson for underwater construction work. In 1843 a Hungarian surgeon, Pravaz, first performed surgery under mild degrees of hyperpressure.[3]

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The problems of a possible improvement of anesthesia with hyperpressure were investigated by Fontaine in 1879 when he used an over-pressure of ⅓ to ¼ atmosphere in attempts to improve nitrous oxide anesthesia. Von Schrotter and associates in Austria in 1900 published the first scientific treatise on "caisson disease," or divers "bends," and decompression necessitated by the accumulation of inert gases in the body was established on a sound basis by Haldane about this same time.

The advent of high speed aircraft during recent years has again focused attention on medical problems incident to rapid ascent to higher altitudes. An early pioneer in this field was Henderson, who in 1917 wrote, "In order for bubbles to be formed it is essential . . . that the pressure with which tissues are in equilibrium should be lowered more than half its absolute amount in a few minutes. In the present state of the art of flying it is scarcely possible for an aviator to rise to a height of 20,000 feet where the barometer would be about half that of sea level in a period sufficiently brief to allow bubbles of nitrogen to form in this way. The disorders from which aviators suffer, therefore, are of a different class from those to which workers in compressed air are exposed."[4] It is immediately apparent that Henderson was aware of the possibility of decompression sickness through rapid ascent to high altitudes, but the aircraft of his day posed no serious problems to aviators. Now, however, in the space age, pilots are confronted with the same problem of decompression sickness as we jet them rapidly into the stratosphere, as is the diver in the sea or the personnel in a medical hyperbaric chamber as they emerge from a high pressure environment.

An early proposed medical application for hyperpressure was made in 1941 by Wangensteen and Lovelace when they considered the possible benefit of treating patients with bowel obstruction in a pressure vessel. Experimental studies with dogs were published in 1954 by Cross, but no significant clinical application was made of this method after that time.[5]

The present period of interest in hyperbaric phenomena was ushered in by Boerema and his colleagues in Amsterdam with their publications in 1956, 1959, and 1961.[6-8] A great impetus to this field of experimental work has been added by Illingworth and his colleagues writing from Glasgow of their experience in the treatment chamber at the Western Infirmary.[9] Specific applications of hyperbaric conditions to various disease states are now under investigation in several centers in the United States as well as in those already established in Europe.

Chamber Design

To accomplish flexibility of operation the Minneapolis hyperbaric unit contains three large chambers and one entrance lock. A central sphere, 19 feet in diameter, functions as a formal operating room and is connected on opposite sides to horizontal chambers which are nine feet in diameter and 18 feet in length (Figure 1) (Also cover). One horizontal chamber is separated from the operating sphere by the entrance lock, and this chamber and lock are designed for operation at seven atmospheres absolute pressure. The spherical operating room and the opposite horizontal chamber are constructed for a maximum operating pressure of four atmospheres absolute. With double doors between all chambers as they are connected in series it is possible to use any one chamber independently of the others or to use them in any combination desired at any given time.

The chambers are constructed of welded steel plate, and the entrance doors are rectangular in shape with a height of six feet and a width of 30 inches. Movement of patients and equipment between the chambers is facilitated by pneumatic floor ramps before each door to adjust for the differential elevations at the bulkheads (Figure 2). A medical "pass-through" lock is provided for each chamber, which is large enough to accommodate standard surgical packs and small-sized gas cylinders (Figure 1). The two chambers designed for operation at seven atmospheres absolute pressure were hydro-

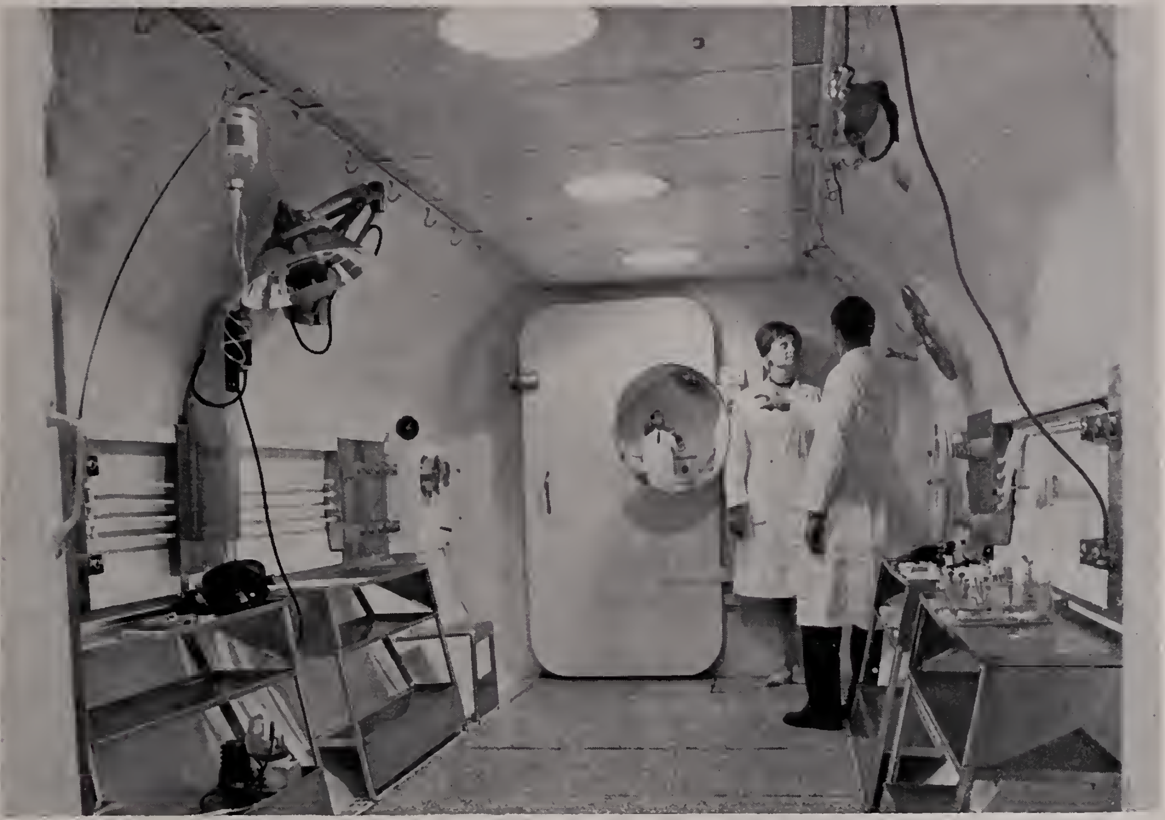

Fig. 2

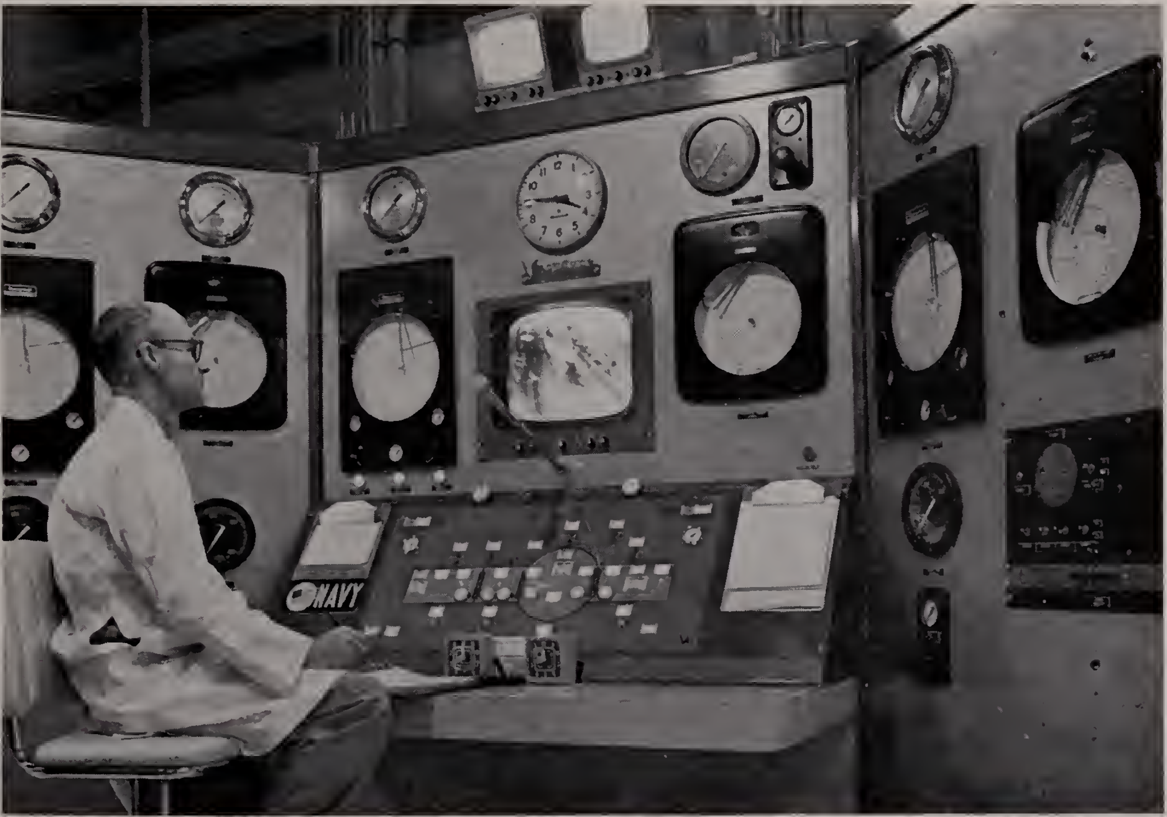

Fig. 3

statically tested with an inside pressure of 10 atmospheres (gauge), and the chambers designed for a maximum operating pressure of four atmospheres were tested with six atmospheres (gauge) inside pressure.

Methods for Pressurizing the Chambers

During ordinary operation the chambers are pressurized with outside air by one of two compressors of the horizontal reciprocating piston type and containing Teflon rings. The output of these compressors is rated at 198, and 160 standard cubic feet per minute. The air inlet is situated 50 feet above the ground (removed from carbon monoxide contamination) and contains filters to remove any particulate matter. The heat of compression is removed from the compressed air as it passes to the chambers through a system of pre-coolers, and final temperature control is effected within each chamber by a built-in air conditioning unit. Chilled brine circulates within these air conditioners and is supplied from a refrigeration unit in the mechanical room. Using one compressor for a given cycle of pressurization, either horizontal treatment chamber can be pressurized to three atmospheres absolute within eight minutes. More rapid pressurization is possible by using both compressors simultaneously.

Adequate ventilation of hyperbaric medical chambers is important for the safety of personnel involved. The Minneapolis unit can be ventilated, with all four chambers at three atmospheres absolute pressure, with a total of 600 standard cubic feet of air per minute. This will permit 20 standard cubic feet of air per minute for the ventilation of each of 10 persons within each of the three major chambers at any one time. Air enters the chambers at the top through inconspicuous grills and discharges at the bottom along the edges of the floor. There is no discomfort or noticeable flow of air during operation of any of the units.

For protection during an electrical power failure or mechanical failure of the compressors, a large volume of air (26,000 cubic feet) is stored in steel cylinders at 3000 pounds per square inch pressure. This high pressure "stored" air is connected for automatic discharge into the pressure system of the chambers in the event of operational failure, and will service one chamber for 12 hours. Anticipating the necessity of treating patients with the "bends" the entrance lock can be pressurized to seven atmospheres absolute within two to three minutes by using both air compressors simultaneously, or mechanically drawing air from the high pressure "stored" source. During chamber operation the flow of pressurized air to the chambers, once established by the operator, is automatically maintained by mechanical modulating valves. Pressure, temperature, and humidity of the air are constantly recorded on separate potentiometers for each chamber during all phases of operation.

Control System

Controls for the Minneapolis facility are semiautomatic and of a combined pneumatic and electrical type. Complete control during chamber operation is centered outside the chambers at a central control panel (Figure 3) and chamber operation is constantly monitored through a closed circuit television system. It is not necessary for the chamber operator to leave his station at any time. In addition to the visual contact through television the console operator is in constant communication with the personnel in each chamber through an intercommunication system. The control console for medical gases (not shown) is immediately to the front of the master control panel and is under constant surveillance by the chamber operator.

Safety Features

Anticipating the possibility of electric power failure, an auxiliary generating unit automatically provides 5000 watts of alternating current to activate the control systems and lights of the hyperbaric chambers and surrounding building. With the already described high pressure air system for chamber operation during emergency conditions, a total power failure can be accepted for many hours without interfering with work in progress within the chambers.

A high-pressure sprinkler system installed in each chamber can be activated either from inside the chamber or from an outside source. This provides a spray of water to all areas of the chamber in the event of fire or explosion. A complete set of auxiliary manual controls for chamber operation has been installed on the wall between the compressor room and the chamber room. The basic protocol for chamber operation calls for two operators at all times, and the manual controls can be manipulated during an emergency by one operator who remains in contact with his colleague at the central control panel through a separate telephone into the intercom.

Each medical pass-through lock (Figure 1) is equipped with a separate telephone connected to the loudspeaker system within the chamber serviced by that lock. Constant communication during a pass-through procedure minimizes any danger of malfunction.

Special Features

Hot and cold running water has been provided in each major chamber. A pressure of 120 lbs. per square inch maintained on this water supply at all times assures entrance of the water into the chamber irrespective of internal pressures involved. Discharge of waste material is accomplished to the sewer by means of special valves which open upon contact with liquid and close upon contact with air.

The use of closed circuit television viewing of each chamber has permitted an admirable arrangement for teaching classes in hyperbaric medicine. The Navy personnel who operate the hyperbaric unit now teach weekly sessions in the conference room for the orientation of nurses, technicians, and medical students.

Medical Gases

All medical gases piped to the chambers are stored in a separate building along with the high pressure "stored" air. The medical gases provided to the chambers consist of the following: oxygen, nitrogen, helium, special mixture No. 1 (helium 40% — oxygen 60%), special mixture No. 2 (nitrogen 40% — oxygen 60%), and nitrous oxide. These medical gases are reduced in pressure at the central gas control panel (not shown) and enter the chambers at a pressure, maintained by a system of differential control regulators, of 50 lbs. per square inch over the internal pressure within the chamber at any given time. Plug-in outlets within each chamber (as seen in Figure 2) permit demand regulator valves to be used with tight fitting masks for gas supply to the patients and technical personnel. A differential vacuum system in the gas control panel also provides a constant level of differential negative pressure for surgical suction. Alarm signals and lights are located on the gas control panel to warn of decreases in pressure within the tubes or faulty operation of the system.

Basic Physical Gas Laws Underlying Hyperbaric Physiology

The potential benefit of hyperbaric therapy depends upon an increase of physically dissolved oxygen in tissues. The physical gas laws, therefore, form the basis upon which this method of therapy is predicated. Henry's Law (1803) states the relationship of pressure to the solubility of gases, showing that the quantity of a gas dissolved into a liquid increases directly as the pressure exerted on the liquid by the given gas. The law governing a mixture of gases was formulated by Dalton (1807) and states that the quantity of a specific gas dissolved by a liquid depends upon the partial pressure of that particular gas in equilibrium with the liquid. Boyle's Law explains the relationship of gas volume to pressure, stating that, if temperature is constant, the gas volume is inversely proportional to pressure exerted on the gas.

The effects of pressure on the animal or human body must be interpreted in terms of tissues containing mostly liquid, and cavities containing air or gases. Recognizing that liquids are virtually incompressible we realize that the partial pressure of water vapor in the alveolar spaces of the lung is a function of temperature only and is nearly independent of ambient barometric pressure. Thus, it is immediately apparent that a complex organism under pressure in a hyperbaric chamber experiences a build-up of the gases breathed into the lungs in direct relationship to the pressure involved in the chamber itself.

At three atmospheres absolute pressure a subject breathing 100% oxygen from a tightly fitting mask will equilibrate after 12-15 minutes to have a partial pressure of oxygen in the femoral artery blood of approximately 2160 mm.Hg. It is this tremendous increase in partial pressure of oxygen available to the blood of the pulmonary capillaries which provides the physiological basis for the possible benefits of tissue "saturation" with oxygen. Under these conditions, all tissues of the body perfused from an intact circulatory system are saturated with physically dissolved oxygen from the plasma and interstitial fluid, and hemoglobin is not required for oxygen transport. The movement of carbon dioxide to the lungs for exhalation, however, does depend on the hemoglobin oxyhemoglobin system for optimum function, even under three or four atmospheres absolute pressure.

It is axiomatic, however, that tissues must be perfused in order to participate in a "saturation" process. Also, serious right to left shunts within the heart and lungs seriously reduce the possible build-up of physically dissolved oxygen in the circulating blood. However, in infants cyanotic from tetralogy of Fallot, pulmonary atresia, or transposition of the great vessels, treatment with 100% oxygen under three or four atmospheres absolute pressure accomplishes a more normal degree of oxygenation of the red cell mass and an improvement of the general condition for a period of time, permitting corrective or ameliorating surgery to be more safely performed.

Study of a normal dog breathing 100% oxygen under three atmospheres pressure reveals an alveolar Po_2 of 2172 mm.Hg (137 mm.Hg partial pressure in room air), an arterial Po_2 of 1975 mm.Hg (63 mm.Hg partial pressure in room air), a venous Po_2 of 89 mm.Hg (25 mm.Hg partial pressure in room air), and a Po_2 in the thoracic duct lymph of 588 mm.Hg (45 mm.Hg partial pressure in room air).[10]

Discussion

Large increases of oxygen in the animal or human body are not without attendant dangers. Oxygen toxicity has been recognized for many years and is still an unsolved problem. Current evidence indicates the likelihood that the central nervous system is the probable seat of the disturbing effects of muscular twitchings and convulsions. Normal human subjects breathing 100% oxygen at four atmospheres absolute pressure can rarely exceed 30-45 minutes without significant danger of convulsions. At three atmospheres absolute pressure the safe time for most normal subjects is extended to approximately three hours. At two atmospheres absolute pressure (one atmosphere over-pressure) subjects will tolerate the increased oxygen concentration for as long as 48 hours.

There is an inverse relationship between the time factor and the oxygen concentration to which the lungs are exposed. The partial pressure of oxygen in the blood and tissues is the critical factor. Thus, 100% oxygen at lower pressures would have the same effect as lower concentrations of oxygen at higher pressures for a given period of time. High oxygen concentrations for prolonged periods of time also have a deleterious effect on the lungs and the mucosa of the tracheobronchial tree. Considerable controversy still exists over these basic phenomena and further research studies will be necessary for more detailed delineation of the pathophysiology involved.

The Minneapolis hyperbaric research team is now engaged in a basic and clinical research program on a 24-hour basis. During the first six months of operation six patients have been treated for gas gangrene. Surgical debridement of the muscle involved with clostridium Welchii infection, plus hyperbaric oxygen at three atmospheres absolute pressure, and penicillin therapy have proved effective in bringing these infections under control. Best results will be achieved, however, if such patients can be treated immediately, once the diagnosis has been established. The clinical picture of clostridial myositis with toxemia, leukocytsosis, and high fever should be taken as an indication for therapy with hyperbaric oxygen. Four of our six patients have recovered uneventfully and one who expired was in a state of extremis upon arrival at the hospital; although improvement was noted following the first three-hour treatment in the chamber, the patient expired with a high potassium level (over 9 mg.%) due to excessive red cell destruction by the circulating toxins.

Since in vitro studies indicate that other infections may benefit from hyperbaric oxygen therapy, it is important that clinical investigation be more thoroughly pursued. The problem of tuberculosis also needs research emphasis as the months go by.[11]

Infants with seriously crippling heart disease such as those with tetralogy of Fallot, pulmonary atresia, transposition of the great vessels and tricuspid atresia can be quickly improved when treated with hyperbaric oxygen; surgery can be performed more safely under these improved conditions.

Other Areas of Likely Research in Hyperbaric Medicine

Other areas of likely research are as follows:

1. Acute respiratory insufficiency (for example the patient with traumatic wet lung and serious pulmonary edema, or the patient suffering from bilateral chemical pneumonia or aspiration pneumonia).
2. Patients with ischemia problems such as myocardial infarction, cerebral vascular occlusion, mesenteric artery occlusion, and vascular injuries in the extremities.
3. Patients with hypovolemic or septic shock.
4. Patients with carbon monoxide poisoning.
5. Cancer; a program of research is underway testing the possible abetment of the action of anticancer agents with hyperbaric oxygenation.
6. Organ grafting. The Minneapolis chambers are now used for harvesting kidneys from human cadavers. Immediately upon death a cadaver placed within the chamber under three atmospheres pressure is perfused with a pump oxygenator using the femoral artery in one leg and both femoral veins. With cross-clamping of the aorta at the level of the diaphragm the kidneys are perfused with blood carrying a Po_2 of 2000 mm.Hg or more partial pressure of oxygen. It is possible, under these conditions, to harvest organs after many hours of ischemia time (three or more) with an improved function upon vascularization within the recipient.

Preliminary studies in the laboratories of our research foundation have indicated a 43% improvement in the healing of experimental wounds in dogs when the animals are treated with hyperbaric oxygenation for the first four days post incision. This area of work needs to be expanded and to also include the potential of hyperbaric oxygen in the healing of fractures.[12,13]

Caution must be the byword for those working in the field of hyperbaric medicine. Ordinarily, the patient is the only person to be considered regarding safety and morbidity inherent in a given method or procedure. However, in the case of hyperbaric oxygenation, either as therapy or as an adjunct to surgery, far greater problems are encountered. Everyone involved, including the medical and paramedical personnel as well as all individuals and property in the surrounding area, can be jeopardized with an improperly constructed or operated hyperbaric facility. It is incumbent upon all who enter this field to do so forearmed with as much basic knowledge of the problems involved as possible. We are pleased to provide the hyperbaric research facility at the Hennepin County General Hospital to the communities of the Central Northwest for the advancement of medical and surgical knowledge.

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One of the Surgical Operations on President Cleveland in 1893

(As Narrated by W. W. Keen)

Doctor Hasbrouck first extracted the two left upper biscuspid teeth (very badly ulcerated) under nitrous oxide. Doctor Bryant then made the necessary incisions in the roof of the mouth, also under nitrous oxide.

At one-fourteen P.M. ether was given by Doctor O'Reilly. During the entire operation Doctor Janeway kept close watch upon the pulse and general condition. Doctor Bryant performed the operation, assisted by myself and Doctor Erdmann.

The entire left upper jaw was removed from the first bicuspid tooth to just beyond the last molar, and nearly up to the middle line. The floor of the orbit — the cavity containing the eyeball — was not removed, as it had not been attacked. A small portion of the soft palate was removed. This extensive operation was decided upon because we found that the antrum — the large hollow cavity in the upper jaw — was partly filled by a gelatinous mass, evidently a sarcoma. This diagnosis was later confirmed by Dr. William H. Welch, of the Johns Hopkins Hospital, who had also examined the former specimens.

The entire operation was done within the mouth, without any external incision, by means of a cheek retractor, the most useful instrument I have ever seen for such an operation, which I had brought back with me from Paris in 1866. The retention of the floor of the orbit prevented any displacement of the eyeball. This normal appearance of the eye, the normal voice, and especially the absence of any external scar, greatly aided in keeping the operation an entire secret.

Only one blood vessel was tied. Pressure, hot water, and at one point the galvanocautery, checked the bleeding. The hemorrhage was not large, probably about six ounces — say, a tumblerful — in all. At the close of the operation, at one-fifty P.M., the pulse was only eighty. The large cavity was packed with gauze to arrest the subsequent moderate oozing of blood. At two-fifty-five P.M. a hypodermic of one-sixth of a grain of morphine was given — the only narcotic administered at any time.

What a sigh of intense relief we surgeons breathed when the patient was once more safe in bed can hardly be imagined!*

---

*Rapport, Samuel, and Wright, Helen: Great Adventures in Medicine. The Dial Press, New York, p. 477-478, 1952.

LOMOTIL®

Each tablet and each 5 cc. of liquid contains:

diphenoxylate hydrochloride	2.5 mg.
(Warning: May be habit forming)	
atropine sulfate	0.025 mg.

- lowers motility promptly
- relieves spasm promptly
- stops diarrhea promptly

Lomotil fulfills the first order of treatment in most patients with diarrhea – prompt symptomatic control.

Pending discovery of the cause, early cessation of diarrhea is almost always urgently indicated. Prompt symptomatic control averts distress, dehydration and, frequently, severe exhaustion.

Both experimental and clinical evidence indicates that Lomotil exerts such control efficiently, safely and with maximal promptness.

dosage:

The recommended initial *adult* dosage is two tablets (2.5 mg. each) three or four times daily, reduced to meet the requirements of each patient as soon as the diarrhea is controlled. Maintenance dosage may be as low as two tablets daily. *Children's* daily dosage (in divided doses) varies from 3 mg. for a child of 3 to 6 months, to 10 mg. for one 8 to 12 years of age.

cautions and side effects:

Lomotil is an exempt narcotic; its abuse liability is low and comparable to that of codeine. Recommended dosages should not be exceeded. Side effects are relatively uncommon but among those reported are gastrointestinal irritation, sedation, dizziness, cutaneous manifestations, restlessness and insomnia. Lomotil should be used with caution in patients with impaired liver function and in patients taking addicting drugs or barbiturates.

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President's Letter

From the time of his election in May until he assumes the duties of his office on the first day of January, the president-elect of the Minnesota State Medical Association has time to reflect on his responsibilities. He usually has had years of experience in committee or council activity and has observed the work of previous presidents. I have had the good fortune to serve for several years in the council where the accomplishments of dedicated and able presidents have inspired me. Upon their experience and sound advice I shall rely heavily. Although the president sits with council, he does not vote. He is not primarily involved in policy decisions, which are the province of the House of Delegates and are carried out by the council.

As I have interpreted the duties of the president, he has three primary areas of responsibility. He serves as the chairman of the scientific program committee. This means that he must begin planning for the May meeting before he assumes office. I hope that the coming program will prove stimulating enough to attract all of our members to the meeting in Minneapolis in May, 1965. The president also must appoint certain committees that will function during the year of his tenure. This is an important task and will be the subject of a subsequent letter. Perhaps the most difficult of the president's duties is to represent the Association as he listens to the deliberation of the House of Delegates and the council and serves as spokesman both to the Association and for the Association in professional and public relationships. It is obvious that to discharge these duties adequately, the president must be informed and he should be accessible to all who have a legitimate call for his ear or his voice.

One of my first interests as your president-elect was to review the components of the State Medical Association. Who are the physicians who make up this organization? In September, 1964, there were 3893 members from a total of 4993 licensed physicians in Minnesota. The directory of the American Medical Association indicates that approximately 45 per cent are in specialty practice and 55 per cent in general practice. There are more than 150 groups of three or more physicians; about 20 per cent of these groups involve a single specialty. As physicians from a state with outstanding schools of undergraduate and graduate medical education, we have an increasing number of faculty and students who are regular or residency members. The physicians who staff our state and federal medical institutions are a relatively small but significant portion of the

Continued on Page 128

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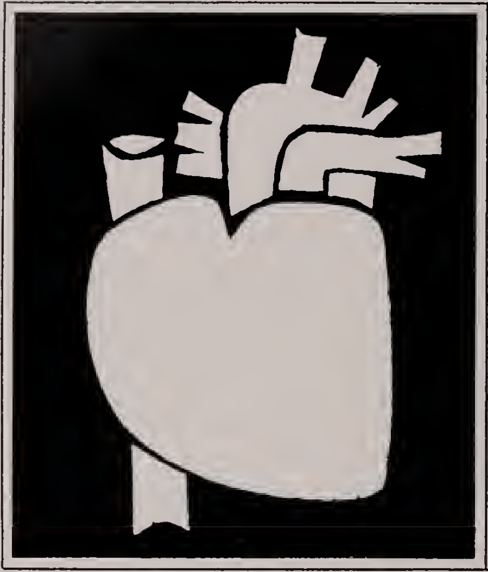

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prophylaxis of pain in angina pectoris

Indications: 'Miltrate' is useful for prophylaxis of pain in angina pectoris and coronary insufficiency, especially where anxiety is a factor. **Contraindications:** Like all nitrates, pentaerythritol tetranitrate should be avoided or prescribed cautiously for patients with glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use. **Precautions:** *Meprobamate* —Patients engaged in activities requiring alertness should be warned of drowsiness. Meprobamate may increase the effects of excessive alcohol, and the possibility of dependence should be considered, particularly in patients with a history of drug or alcohol addiction. Sudden withdrawal may result in reactions, rarely epileptiform seizures. Grand mal attacks may be precipitated in persons susceptible to both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies. **Side effects:** *Pentaerythritol tetranitrate*—The most common side effects are transient headache, nausea, and rash. Weakness, palpitation, flushing, gastrointestinal distress, and lightheadedness have been reported on a few occasions. *Meprobamate* —May cause drowsiness and, rarely, ataxia, usually controlled by decreasing the dosage. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses of the drug. Mild reactions include urticarial or maculopapular rash. Serious reactions, rarely encountered, include dermatological effects, acute nonthrombocytopenic purpura, chills, fever, fainting spells, angioneurotic edema, bronchial spasm, hypotensive crisis, anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic, and the drug not be reinstituted. **Dosage:** Usual dosage is one or two tablets before meals and at bedtime. Individualization of dosage is required for maximum therapeutic effect. Doses above twelve tablets daily are not recommended. **Supplied:** White tablets, each containing meprobamate 200 mg. and pentaerythritol tetranitrate 10 mg. *Before prescribing, consult package circular.*

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Editorials

The Gold Headed Cane Tradition

FIVE RETIRING medical staff members from the Mount Sinai Hospital were given distinctive canes at an honorary dinner upon retirement from the active staff: Drs. Moses Barron, Samuel Dworsky, Charles Hymes, Virgil Schwartz, and Max Seham. In the presentation of the canes, the history of the London gold-headed cane was reviewed:

"From the time of antiquity the staff, rod or cane has been associated with the lore and art of medicine. Our modern symbol of medicine, the caduceus, bears the winged staff of Mercury, the intermediary between man and the Gods, around which is wrapped a serpent to portray the renewal of life after illness or shedding of the skin. Probably the most famous biblical reference to this association of medicine is the shepherd's staff from the 23rd Psalm. 'Thy rod and thy staff they comfort me.' The physician is in many a sense the shepherd whose staff restoreth both body and soul.

"In more modern times the famous Gold-Headed Cane of London became the hallmark and mace of leadership in Medical Practice. In 1825 it was presented to the Royal College of Physicians by the widow of Mathew Baillie, the last of the five wearers of the cane. There it remains today, a symbol of an era of excellence in the art and practice of Medicine.

"The first owner of this elegant walking stick was Dr. John Radcliffe who in 1669 was physician to Queen Anne and King William III. Radcliffe's heir apparent and next recipient of the Cane was Richard Mead, who amongst his other accomplishments experimented with small pox vaccination 25 years before Jenner. The third owner of the Cane was Anthony Askew, about whose medical accomplishments little is known. Not much more is known of the fourth custodian of the Cane, Dr. Archibald Pitcairn, other than that his brother, Major Pitcairn was killed at the battle of Bunker Hill. The fifth and last to accept the Cane as the mantle of leadership in medical practice of London was Mathew Baillie, well known anatomist and physician, and nephew of John and William Hunter.

"You gentlemen have brought to our staff strong, diverse, highly individual personalities. Your retirement from active practice will leave a void of personal devotion, individual excellence, and highly developed skills that our generation will find difficult to replace.

"With great pleasure I present to each of you from your many friends and colleagues, this silver-headed walking stick in appreciation of your long, devoted and distinguished service to the best of medicine and medical practice."

Arnold J. Kremen, M.D.
Minneapolis, Minnesota

What an opportunity for reviving a noble tradition, for honorable, deserving, self-sacrificing gentlemen!

What's new at Geigy? Regroton, Doctor. For high blood pressure.

Not *another* reserpine-diuretic combination!

Certainly. Regroton has outperformed other combinations.

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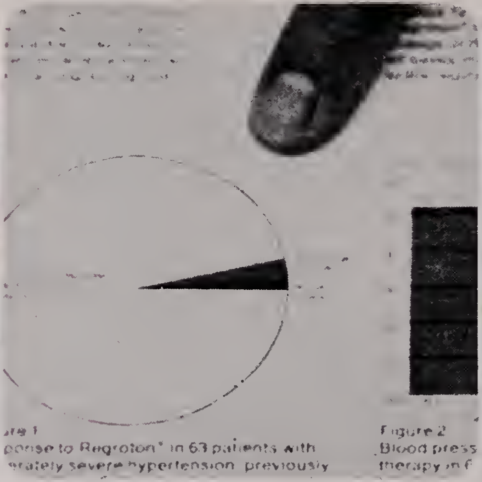

Says this 2-year study by Finnerty.

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That's what they say.

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Contraindications: History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.
Warning: Discontinue 2 weeks before general anesthesia, 1 week before electroshock therapy, and if depression or peptic ulcer occurs.
Precautions: Reduce dosage of concomitant antihypertensive agents by one-half. Discontinue if the BUN rises or liver dysfunction is aggravated. Electrolyte imbalance and potassium depletion may occur; take particular care in cirrhosis or severe ischemic heart disease, and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended. Use with caution in patients with ulcerative colitis, gallstones, or bronchial asthma.
Side Effects: Nausea, vomiting, diarrhea, muscle cramps, headaches and dizziness. Potential side effects include angina pectoris, anxiety, depression, drowsiness, hyperglycemia, hyperuricemia, lassitude, leukopenia, nasal stuffiness, nightmare, purpura, urticaria, and weakness.
For full details, see the complete prescribing information.

Availability: Bottles of 100 and 1000 tablets.
Average Dosage: One tablet daily with breakfast.

*Chupkovich, V.; Finnerty, F. A., Jr., and Kakaviatos, N.: The value of chlorthalidone plus reserpine in moderately severe and severe hypertension: A two year study. Presented at the 7th Inter-American Congress of Cardiology, Montreal, June 14–19, 1964.

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Hemochromatosis*

THE ARTICLE on hemochromatosis by Watson and Murray* is noteworthy since these authors express their views without hesitation on the most sensitive and controversial issues in the pathogenesis of the disease. They point out that although Bell, in 1944, found varying amounts of hemosiderin in the livers of patients with cirrhosis and diabetes, he did not call these true hemochromatosis. They also refer to Bell's discussion of a type of hemochromatosis associated with severe anemia in patients who had not received a significant number of blood transfusions. In 1954, we emphasized this type of "secondary hemochromatosis" associated with chronic anemia, which is now well recognized as being distinct from the primary form.

Watson and Murray without question accept the concept that there is a primary type of hemochromatosis and that the hemochromatosis in some of these cases is hereditary. These authors are perhaps the first to strongly refute the concept of MacDonald, who believes that there are no familial or genetic relationships and who has proposed that idiopathic hemochromatosis is a variant of portal cirrhosis with an alcoholic or nutritional cause. Watson and Murray lucidly present the available data, pointing out the reported low incidence of alcoholism as compared to MacDonald's figure of 85 per cent in the Boston series. Certainly, the opinions expressed by Watson and Murray are similar to my observations of 55 patients living mainly in the central United States in whom alcoholism was noted only in a minor percentage and the use of wine, especially, was rare. Our experience reveals that approximately 50 per cent of patients with primary hemochromatosis have "normal" liver function tests, which certainly is a contrast to the group reported by MacDonald in which jaundice was found in 39 per cent. In primary hemochromatosis, jaundice is exceedingly rare except when complicated by a hepatoma. The issue of fatty liver as reviewed by Watson and Murray agrees with my own views; in my experience this is a rare finding in primary hemochromatosis, even with severe diabetes. The observation of heavy deposition of iron in the cirrhotic liver after portacaval shunts is commented on by Watson and Murray, who include a case report of their own. Dr. Bell might have commented on MacDonald's series by a summary in his textbook in 1947 as follows, "Moderate amounts of hemosiderin are frequently found in the liver in ordinary cases of portal cirrhosis, and sometimes the degree of pigmentation approaches that which we are accustomed to consider characteristic of hemochromatosis." This latter group might be called the "MacDonald type" and, as mentioned by Watson and Murray, could be considered a form of acquired hemosiderosis in contrast to primary hemochromatosis.

An excerpt from MacDonald's article, "since iron is not the cause of hemochromatosis, but merely colors our livers and our thinking —," expresses his view on the doubtful role of iron in the etiology. The dramatic improvement in the status of some patients with primary hemochromatosis with diminution of liver size and return of normal activity after multiple phlebotomies is evidence of the pathologic effects of large amounts of iron in the body.

Maurice H. Stauffer, M.D.
Rochester, Minnesota

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*Watson, C. J., and Murray, M. J.: Hemochromatosis. Minnesota Med, 47:10:1177.

Reference

1. Stauffer, M. H., Butt, H. R., and Dockerty, M. B.: Hemochromatosis: Clinical Features and Methods of Diagnosis in 27 Cases. Gastroenterology 27: 31, 1954.

Don't put too fine a point to your wit for fear it should get blunted.—Cervantes

ONE WAY TO TRY TO
AVOID COLDS AND
SINUSITIS IS TO
GET AWAY FROM
FRIGID WEATHER

...but if your patient can't get away, relieve sneezing, running nose, and congestion of colds and sinusitis all day or all night with one

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Summary of contraindications, cautions and side effects: Do not use in patients with glaucoma, prostatic hypertrophy, stenosing peptic ulcer, pyloric duodenal obstruction, or bladder neck obstruction. Use with caution in the presence of hypertension, hyperthyroidism, or coronary artery-disease. Drowsiness; excessive dryness of nose, throat or mouth; nervousness or insomnia may occur on rare occasions but are usually mild and transitory.

Before prescribing, see SK&F Product Prescribing Information.

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Fatal Neoplasms

A CAREFUL analysis has been made of the frequency, types, and age and sex distribution of fatal neoplasms diagnosed at necropsy at the University of Minnesota in a 51-year period. Although Dr. Robert Hebbel* thoughtfully discusses the limitations of a study of this type, many workers consider data of this kind superior to that obtained from other sources. Certainly this report appears to reflect accurately the trends of fatal neoplastic disease in a large metropolitan area; most of the findings confirm commonly held concepts of neoplastic disease. Although the data were not subjected to statistical analysis, an increased incidence of lung cancer in men was definitely observed in the later years covered by this study. The over-all high incidence of leukemias, lymphomas, and gliomas is worthy of note.

Jack L. Titus, M.D.
Rochester, Minn.

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*Hebbel, Robert: Fatal Neoplasms, 1911-1962. Minnesota Med 47:1227.

Allergy and Purpura

SOME OF the difficulties in demonstrating allergic mechanisms in disease of man are described by Bowie and Hagedorn in a discussion of allergic aspects of purpura elsewhere in this journal.* In each of the major types of allergic purpura there are differences of opinion as to whether allergic mechanisms operate and, if so, as to the exact nature of the altered response.

Anaphylactoid purpura, once considered to be clearly related to streptococcal infection, is now thought to represent a form of delayed hypersensitivity to a wide variety of infections, as well as to many other agents, including foods, drugs, insect bites, etc. Studies also suggest that in some instances it may represent a type of autoimmune response to vascular endothelium. The exact role of these various agents is not established.

The role of allergy and immunity in idiopathic thrombocytopenic purpura is even more widely disputed. Opinion varies from the suggestion that it should be renamed autoimmune thrombocytopenic purpura to a denial of autoimmunity as an etiologic factor. It is clear that something in the blood of patients with idiopathic thrombocytopenic purpura depresses platelet counts in normal persons, but it is less clear that this represents an antigen-antibody reaction. Many techniques for demonstrating antibody give negative results in patients with idiopathic thrombocytopenic purpura and there are reasons to question results from techniques which have been said to give positive results. Whether these facts argue against an immunologic basis or are merely a reflection of the inadequacy of testing methods cannot be answered at this time.

Finally, the pathogenesis of drug-induced purpura is not much clearer. It appears that some drugs, not in themselves antigenic, bind to serum protein, and the combination is thought to have antigenic specificity. This is considered to be the mechanism of quinidine-induced thrombocytopenia and has been proposed by some as the mechanism for chlorothiazide-induced thrombocytopenia.

A wide variety of agents are related in some way to the clinical manifestation purpura, but the exact nature of these relationships is not always clear.

Robert A. Green, M.D.
St. Louis Park, Minnesota

the problem: diabetic . . . overweight . . . unresponsive to diet alone

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side effects: Gastrointestinal, occurring more often at higher dosage levels, abate promptly upon dosage reduction or temporary withdrawal. **precautions:** Occasionally an insulin-dependent patient will show "starvation" ketosis (acetonuria without hyperglycemia) which must be differentiated from "insulin-lack" ketosis which is accompanied by acidosis, and treated accordingly. Lactic acidosis has been reported in nondiabetics and diabetics treated with insulin, with diet, and with DBI. Question has arisen regarding possible contribution of DBI to lactic acidosis in patients with renal impairment and azotemia and also those with severe hypotension secondary to myocardial or bowel infarction. Periodic B.U.N. determinations should be made when DBI is administered in the presence of chronic renal disease. DBI should not be used when there is significant azotemia. Any cardiovascular lesion that could result in severe or sustained hypotension, which may itself lead to development of lactic acidosis, should be considered cause for immediate discontinuation of DBI at least until normal blood pressure has been restored and is maintained without vasopressors. Should lactic acidosis occur from any cause, vigorous attempts should be made to correct circulatory collapse, tissue hypoxia, and pH. **contraindications:** Severe hepatic disease, renal disease with uremia, cardiovascular collapse. Not recommended without insulin in acute complications of diabetes (metabolic acidosis, coma, severe infections, gangrene, surgery). **pregnancy warning:** *During pregnancy, until safety is proved, use of DBI, like other oral hypoglycemic drugs, is to be avoided.* Consult product brochure for full information.

1. Faludi, G.: J. Am. Med. Women's Assoc. 18:722, 1963. 2. Weller, C. et al.: Scientific Exhibit, A.M.A., June, 1962. 3 Moss, J. M. et al.: Medical Times 92:645, 1964.

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Letter to the Editor:

It distresses me to see that, in spite of overwhelming evidence that nobody can afford to smoke, many still keep on smoking. Not many are really making a determined effort to stop this exceedingly dangerous habit. Everybody should try to quit and nobody with good intelligence will start the habit, now that the results of years of research have at long last been well publicized. Years ago I called smoking an addiction, but until recently other doctors were not in agreement with me.

For five years prior to 1938, while studying in the Barnard Free Skin and Cancer Hospital of St. Louis and in the New York Skin and Cancer Hospital, I took smoking histories on all cases diagnosed cancer of the lungs. Earlier, I had been for 2½ years just after World War I a chest patient in army and civilian hospitals where I saw a number of associates and good friends die of lung cancer. This caused me to be intensely interested in whether lung cancer was directly related to smoking.

I was forced to conclude from my five years of smoking histories on lung and heart cases even before 1938 that everyone who smokes at all should have a fear of lung cancer, heart disease, and cancer of the lip, throat, mouth, larynx, epiglottis, and esophagus. Those who had these cancers were almost without exception smokers.

For over 25 years now I have with too little success tried to convince the reading public that nobody can afford to smoke. The greatest resistance comes, I am afraid, from smoking publishers and editors and from those who successfully promote smoking through their newspaper.

I have often felt like a lamb bleating in the face of a Minnesota blizzard.

Adrian H. Scolten, M.D.
Portland, Maine

The Editor's Soliloquy

No, Thanks

In popular magazines one often reads of a new way to quit smoking, or of a diet for those who cannot reduce, or of a pattern of life for those who drink too much, or of a method of correcting bad habits, and of a thousand and one other things designed to eliminate our ever-present human dissipations.

Do we need these props? Is it not enough to know that intemperance of smoking, overeating, alcoholism, bad habits, and all of these excesses we humans keep trying to curb, are bad for our health? Does any other member of the animal kingdom indulge in excesses to the detriment of its health? When our marvelously constructed physiologic body finally succumbs to cancer of the lung (tobacco), or when the liver gives up and becomes cirrhotic (alcohol), or when the blood vessels become arteriosclerotic (overeating), is it not possible or even probable that these diseases developed because we didn't have the courage to say "No" — without compromise or capitulation? Do we need a *new* way of saying no: a new inflection, a new posture? Why not just try saying politely but firmly, *"No, thanks."*

Carl O. Rice, M.D.

Those who want the refuge of idoit bliss can find it in tranquilizing pills or in senility.—Leo Rosten

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Curbstone Consultation

Varicose Ulcers

QUESTION: How do you treat varicose ulcers of the leg?

ANSWER: The basic principles of treatment consist of cleanliness and elevation of the leg or compression by sponge rubber and elastic dressings when the leg is in the dependent position. Local and systemic antibiotics are sometimes needed along with warm wet packs, elevation, and bed rest and even hospitalization in the infected far advanced type of ulcer. An intelligent patient can usually take care of the leg on an ambulatory basis. At times because of the patient's inability to care for the lesion a judiciously and carefully applied gelcast boot with changes weekly or more frequently will effect reduction in size of the ulcer. Surgical treatment of the varicosities and even skin grafting may be necessary at times. The problem requires patience and understanding of the underlying pathology by both patient and physician.

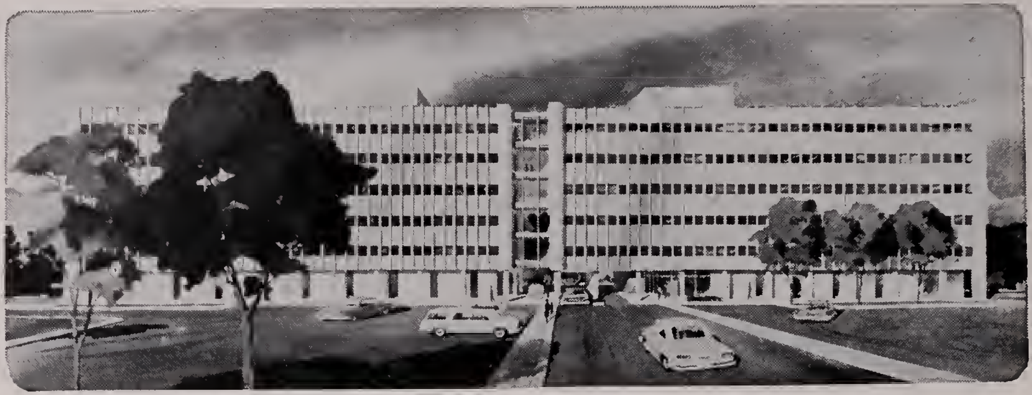
Asymptomatic Pulmonary Nodule

QUESTION: What would you do with a male patient fifty-four years of age who had an asymptomatic pulmonary nodule approximately 2 cm. in size noted on the last chest roentgenogram? Previous chest roentgenograms demonstrate that the nodule was present although perhaps slightly smaller two years prior to the last roentgenogram.

ANSWER: This patient presents the classical problem of the coin lesion. Large studies have shown that if the coin lesion contains calcium and especially if the calcium is dense or concentric, the possibility of this being a peripheral carcinoma is remote. However, in coin lesions that do not demonstrate any evidence of calcium on laminography, approximately 50% in males over fifty years of age will prove to be carcinomas. Even though this lesion has been present for two years this is not inconsistent with a peripheral carcinoma, as X rays have shown lesions present as long as seven years which were actually peripheral carcinomas. Therefore, this individual should have further studies in the form of laminography, exfoliative cytologic studies, bronchoscopy (although this is not to view the lesion but rather to study the tracheal bronchial tree in detail to rule out other lesions). If the lesion is without calcium an exploratory thoracotomy is indicated.

To cure nine out of ten neuroses, take hard work in heavy doses.

—Cincinnati Enquirer



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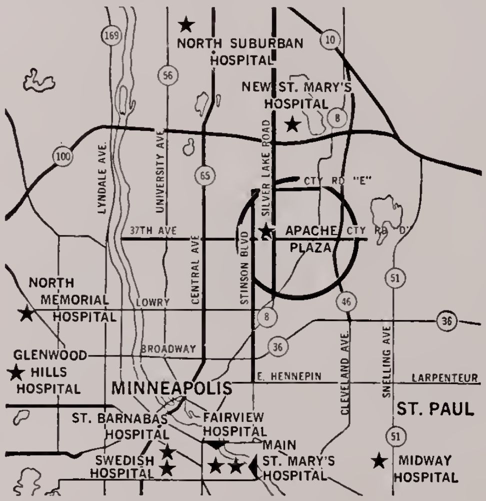
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Fracture–Trauma Conference

Immobilization in Fractures of the Fingers

What appear to be relatively minor fractures of fingers can sometimes result in rather markedly severe deformities and limitations of hand function. The primary concern of the surgeon in treating fractures of the hand is to obtain good function of the hand subsequent to treatment. It is especially important to be careful to avoid limitation of motion in joints that are not involved in the fracture itself. In addition, it is important to carefully avoid rotational deformities or angulation.

Fractures of this type in growing children differ somewhat from those in adults in that deformities will often correct themselves by the normal growth of the bone. This is especially true of angulatory deformities in which the angle of the deformity is in the same plane as the angle of motion of the adjacent joints; it is also partially true of angular deformities in the opposite plane. Rotational deformities, however, will not be corrected by growth.

In treating fractured phalanges, the best method of treatment is usually to reduce the fracture under anesthesia and then hold the injured finger along with its adjacent finger or fingers in the "position of function," or as is sometimes called, the "position of rest." Rotation can be controlled by being sure the immobilized digit points toward the carpal navicular. If the fracture is unstable in this position, then internal fixation with Kirschner wires or Steinman pins should be used. The pins can usually be placed in a crossed fashion over the fracture site without involving the adjacent joints. Occasionally, a pin in the intermedullary canal will immobilize the fracture better.

Utilizing skin traction, pulp traction, or skeletal traction for a fracture of the phalanx is ordinarily not a good choice of treatment. The reason for this is that, despite the fact that the traction will often provide good immobilization as well as excellent alignment, it may result in limitation of motion of adjacent joints. It is impossible to mobilize the adjacent joints of the hand while the finger is in traction. In addition, it is somewhat difficult to hold the finger in the ideal position of rest during immobilization. There is also the possibility that the pull of the traction through the adjacent joints may result in over-stretching and scarring of the capsular structures of the joints not involved in the injured area.

Continued

When the internal fixation method is used, the pins can be placed in such a fashion that all the adjacent joints can move. As a result, motion can be started much earlier. Ordinarily, the small pins will be removed after the fracture is healed.

The time required for immobilization of a fracture in the hand is determined as in other parts of the body by the age of the patient and the type of fracture involved. A youngster will ordinarily heal one of these fractures more quickly than an older patient. A transverse, undisplaced fracture will heal more quickly than a comminuted or spiral oblique fracture.

It is necessary to follow these fractures closely with X rays at frequent intervals. When the fracture shows evidence of adequate progression of healing, early motion of the adjacent joints of the finger and hand should be begun. When the fracture is solid clinically and by X ray, active range of motion in the involved parts should be instituted immediately. Only after the fracture has completely solidified and all edema and soreness has subsided, should passive range of motion of the fingers be used.

Case Report

This is a report of a 17-year-old patient from Hennepin County General Hospital who sustained a fracture-epiphyseal separation of the base of the proximal phalanx of his ring finger. The fracture was initially treated and reduced by utilizing skeletal traction in the middle phalanx of his finger. The forearm and wrist were then immobilized with a cast, and traction was applied from the finger to the volar aspect of the cast. The finger was held in acceptable position. The reduction of the fracture-epiphyseal separation in the traction was excellent. The patient also had a fracture of the base of the proximal phalanx of the fifth finger of the hand which was immobilized in the position of rest on a volar splint.

After four weeks, the traction was removed and the finger was begun on active range of motion.

The patient was seen ten weeks after the fracture, and X ray showed healing of the fracture in excellent position. Function of the hand, however, was unsatisfactory! The patient had a 90-degree flexion contracture of the *proximal interphalangeal joint* of that finger. It is important to note that the injury did not involve this joint and that, in fact, it involved the opposite end of the proximal phalanx.

Discussion

This case demonstrates that despite excellent reduction and adequate immobilization for the proper period of time in the proper position, the traction method of immobilizing fractures of the phalanges should be avoided unless no other method is available. The present fracture could better have been treated with closed reduction and pinning of the epiphysis with two small crossed wires.

It should also be added that the proximal interphalangeal joint is the most sensitive and delicate joint in the hand, and unnecessary immobilization or traction of this joint should be avoided whenever possible.

Joseph M. Tambornino, M.D.
Minneapolis, Minnesota

To lose one's health renders science null, art inglorious, strength effortless, wealth useless, and eloquence powerless.—Herophilus B.C. 300

Even if we could see ourselves as others see us, we wouldn't believe it.
—Changing Times

Tumor Conference

Villous Adenoma with Electrolyte Imbalance

The first clinical description of a villous tumor was written by Timothy Holmes in 1861.[1] More recently, an association has been demonstrated between these tumors and profuse fluid and electrolyte imbalance. One of the first descriptions of this relationship was written by McKittrick and Wheelock in 1954.[2] In 1961, Davis[3] reviewed the 22 known cases of secreting villous tumors. Since that time a few additional case reports of villous tumors with electrolyte disturbance have been reported.

The following case, a typical example of a secreting villous adenoma, is reported because of the clinical importance in recognizing this syndrome, and because of the apparent rarity of the tumor.

Report of Case

A 69-year-old white female was admitted to the University of Minnesota Hospitals for the first time with the complaint of frequent bowel movements. Approximately five years prior to her admission she first noticed the onset of increasing frequency of bowel movements. She also noticed that with her bowel movements she passed a great volume of clear liquid and occasionally clear liquid alone. These symptoms had increased in frequency until she was having about ten movements a day with rectal urgency. Two months prior to her admission she had developed chills, fever, nausea, and vomiting and was thought to have a rectovesical fistula. Just prior to her admission she had noted profound weakness and stated that she drank a great deal of water and felt thirsty most of the time.

The *physical examination* was unremarkable except for the proctoscopic examination which revealed a large papillary tumor beginning at 9 cm. and which completely filled the bowel lumen at 11 cm.

Numerous *biopsies of the lesion* through the proctoscope revealed adenomatous rectal mucosa histologically. The barium enema revealed a large filling defect on the posterior wall of the rectum and distal sigmoid measuring about 13 cm. in length, which was interpreted as suggestive of malignancy but possibly representing a very large villous adenoma.

Blood chemistries on admission revealed a potassium of 3.0 mEq./L., sodium of 142 mEq./L., chloride of 103 mEq./L., carbon dioxide of 32 mEq./L., and blood urea nitrogen of 33 mg. %. The total serum proteins were 6.4 gr. %. Samples of rectal fluid were collected and found to contain 78 mEq./L. of potassium, 88 mEq./L. of sodium, and 127 mEq./L. of chloride, although the normal average values are potassium 12 mEq./L., sodium 3 mEq./L., and chloride 2 mEq./L. The initial specific gravity of the urine was 1.027. The remainder of the laboratory and radiological examinations were within normal limits.

Continued

The patient's fluid and electrolyte balance were restored employing parenteral and oral routes, following which the patient was operated upon for excision of the tumor. At surgery the tumor was palpated in the distal sigmoid colon as a soft velvet-like mass. A segmental resection of the sigmoid colon with a low anastomosis at the level of the levator ani muscles was carried out.

The *specimen* measured 30 cm. in length (Figure 1). There was an annular soft tumor mass beginning 2 cm. from the distal end of resection and extending 14.5 cm. circumferentially along the bowel. The surface was covered with soft villous structures measuring up to 2 cm. in thickness. The margins were sharp at both extremities. Histologically the tumor was formed of greatly thickened layers of mucous membrane covering thin fibrous stalks (Figure 2). The mucosal glands were greatly elongated and were lined by tall mucus-secreting cells. The stalk showed no evidence of invasion in any section. There was no tumor in the 22 lymph nodes examined. The patient had an

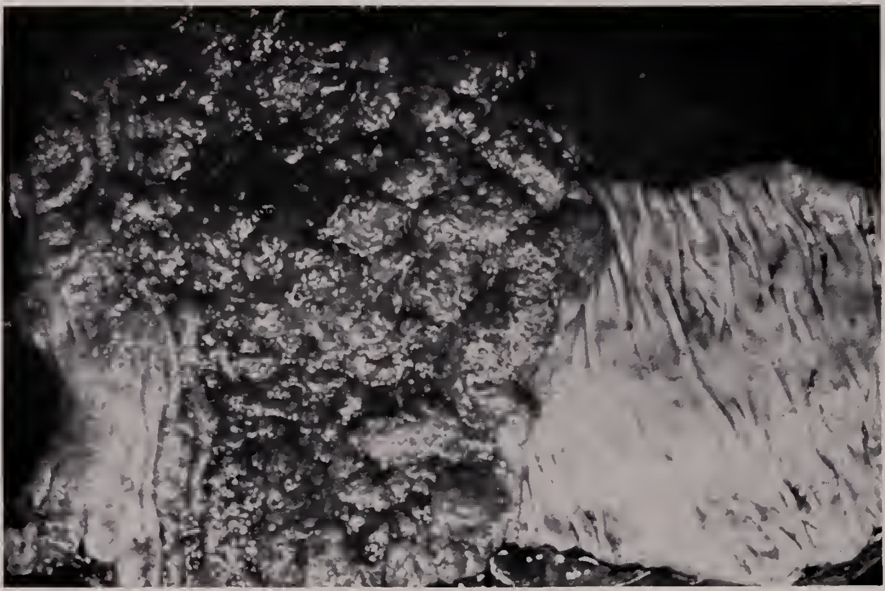

Fig. 1 — Photograph of the gross tumor.

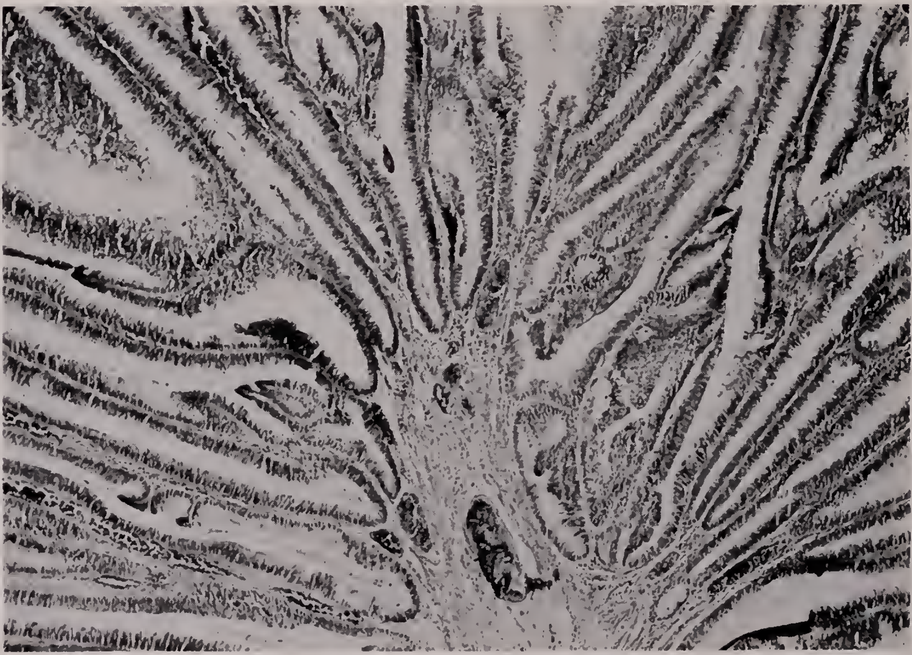

Fig. 2 — Photomicrograph of the villous adenoma (x25) demonstrating finger-like projections arising from a fibrous stalk.

uneventful postoperative course and has had no evidence of recurrence 1.5 years following surgery.

Discussion

Villous tumors account for 1%-3% of surgically removed neoplasms from the colon and rectum. Most are located in the rectum and sigmoid colon.[4]

All villous adenomas produce mucus, but the volume is usually inadequate to produce the symptom of pseudodiarrhea early in the course of the disease. The ability to compensate for the loss of fluids and electrolytes may extend over many years until the tumor enlarges sufficiently, intake is decreased or fluid loss increased to the point where the compensatory mechanisms are ineffectual. At this point, anorexia, weight loss, vomiting, muscular weakness, and severe thirst become prominent. If the patient's course is uninterrupted by treatment, mental confusion, shock, and death may soon follow.

The average duration of symptoms is over five years, and electrolyte imbalance appears to be a late complication.[5] The volume of fluid produced seems to be correlated with the size and surface area of the tumor and to the activity of the surface cells. The area is greatly increased by the convolutions of the frondlike projections inherent in the villous tumor.[3] The rectal fluid appears to be secreted by the cells of the tumor rather than a simple transudate. Shnitka[6] has demonstrated that the average potassium concentration of the rectal fluid is 13.2 times the concentration in serum, though the sodium and chloride approximate serum levels suggesting active secretion of potassium by the cells of the villous tumor. Concurrent depletion of potassium, sodium and chloride with elevation of the BUN and urine specific gravity is the usual picture.[3] The serum proteins are also often depressed, owing to proteinous content of the rectal fluid. This fluid may contain up to 5 gr. of protein per 24 hours.[7]

Symptoms

The most prominent symptom is the profuse rectal discharge passed separately from stool, giving rise to the characteristic pseudodiarrhea.[3] Although the normal water loss in the stool is 100-200 cc. per 24 hours, volumes of up to 3-4 liters per 24 hours can occur, giving rise to the syndrome of dehydration, hypokalemia, uremia, and even death if the electrolyte depletion is not treated.[8] The less frequent symptoms include bleeding, prolapse and intussuception of the tumor, and tenesmus.[3] These tumors are rarely obstructive and are often not palpable by digital examination because of their soft and velvet quality. The barium enema is helpful, especially if the lesion is beyond the reach of the proctoscope.

Malignant Degeneration

Villous tumors have a tendency to undergo malignant degeneration; the incidence ranges from 10%-100% in various series, a discrepancy resulting largely from differing criteria. Biopsying the lesion through the proctoscope is unsatisfactory for, as Dockerty[9] stressed, a carcinoma can lurk in a fold of the tumor and not be found.

Treatment

Treatment consists of restoration of the fluid and electrolyte balance, although this will be difficult to maintain prior to the removal of the

Continued

secreting tumor. Employing whatever procedure is required, complete excision of the lesion with a margin of normal tissue should be carried out as soon as the patient's condition permits.[3] If the lesion is malignant, a cancer operation should be performed.

Robert P. Belin, M.D.*
Minneapolis, Minn.

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*From the Department of Surgery, University of Minnesota Medical School.

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The Penalty of Overweight

Individuals who are overweight suffer from one-fourth to three-fourths excess in mortality. The hazard percentage of obesity can roughly be stated by the same number as the pounds of overweight. Ten pounds of overweight suggests ten per cent increase in the mortality. Twenty pounds overweight suggests twenty per cent increase in the mortality, etc.

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Clinical Path Conference

Back Pain and Herpes Zoster

Report of Case

A 64-year-old white man registered at the Mayo Clinic in May of 1958 and was admitted to the hospital. Six days previously he had developed sudden, severe sharp pain in the region of the seventh thoracic vertebra. The pain was constant and continued until the time of his admission.

The patient had had the onset of backache involving the thoracic region of the spine in the fall of 1957. He had lost 10 pounds since that time. Although he had a nonproductive morning cough, he had experienced no hemoptysis.

Review of symptoms was essentially within normal limits except for a history of duodenal ulcer in 1957.

Physical Findings

At the time of admission, the blood pressure measured 162 mm. Hg systolic and 78 diastolic (162/78), and the pulse rate, 120 beats per minute. A sebaceous cyst measuring 1.5 cm. in diameter and 1.0 cm. high was felt in the right occipitoparietal region of the scalp. Coarse rales were heard on inspiration in both bases of the lungs. There was no visceromegaly. The prostate gland was enlarged, grade 2, and considered to be benign. Deep tendon reflexes and peripheral pulses in the lower extremity were within normal limts. A vesicular eruption was observed over the back along the route of the right seventh thoracic nerve. Exquisite pain was elicited by light touch over the seventh thoracic vertebra.

Laboratory Findings

Blood hemoglobin measured 12.2 gm. per 100 ml. Erythrocytes numbered 4,080,000 per cubic millimeter of blood, and leukocytes numbered 5,000. A differential leukocyte count revealed 79.5 per cent neutrophils, 12.0 per cent monocytes, and 8.5 per cent lymphocytes. The sedimentation rate was 88 mm. in 1 hour (Westergren). Review of the peripheral blood smear revealed rouleaux formation, grade 3, with toxic polynucleosis. Total serum proteins measured 11.0 gm. per 100 ml. and serum globulins, 8.17 gm. Values for serum calcium, phosphorus, and alkaline phosphatase were within normal limits. Roentgenograms of the chest revealed emphysema of both lungs with probable bronchiectasis at the bases; osteolytic lesions were evident in the eighth rib on the right, posteriorly. Roentgenograms of the head revealed multiple osteolytic lesions of the skull.

Clinical Course

The patient continued to complain of pain for two days after his admission to the hospital. His cough progressed and became more productive. On the third day of hospitalization, new herpetic lesions were observed along the routes of the fifth and eighth thoracic nerves. In addition, similar lesions appeared on the face. The patient subsequently became quite drowsy and on the fourth day of hospitalization was found to be in shock. There were marked rales and rhonchi over both lungs. Despite supportive measures, the patient died.

Continued

Discussion of Case

Murray N. Silverstein, M.D.*

In summary, we have for consideration the story of a patient who had severe back pain and a vesicular skin eruption. Coupled with this, he had constitutional manifestations. Laboratory studies revealed an elevation of the sedimentation rate, marked rouleaux formation on the peripheral blood smear, and hyperglobulinemia. It was my impression on seeing this patient that he had multiple myeloma associated with herpes zoster.

Multiple Myeloma vs. Pain

Of the patients with multiple myeloma who were studied at the Mayo Clinic by Doctors Bayrd and Heck, roughly 85 per cent presented with pain. The outstanding site of pain, of course, was the region of the vertebral column; for, since the bony lesions of myeloma are primarily osteolytic and osteoporotic, collapse of vertebrae is quite frequent.

Protein Electrophoretic Pattern

The blood picture in myeloma can be quite variable. Approximately 80 per cent of patients will have anemia at some stage of their disease. Some 35 per cent of patients studied at the Mayo Clinic have had leukopenia on first observation. Serum protein electrophoresis has been diagnostic in at least 65 per cent of our patients, and in 50 per cent, Bence-Jones protein has been found in the urine. Consequently, study of protein electrophoretic patterns of the blood and urine of patients with myeloma should yield positive results in about 95 per cent of cases. Biopsy of bone marrow should be diagnostic in all cases of myeloma except for those few patients who have so-called solitary extramedullary myelomas.

Herpes Zoster with Myeloma

The association of herpes zoster with myeloma is quite infrequent in our experience. We have seen herpes zoster complicating, or associated with, lymphomatous processes in about 8 per cent of our patients with lymphoma. This has been most frequent in the Hodgkins group of lymphomas.

A study of mineral metabolism in myeloma has revealed that about 36 per cent of our patients have had hypercalcemia. A recent review by Dr. Dillman and myself has shown that alkaline phosphatase is elevated in about 14 per cent of patients with myeloma.

An examination of the bone marrow was performed in the case under consideration. The marrow was found to be cellular, and many myeloma cells were present.

The patient had a most unusual clinical course for multiple myeloma, particularly with respect to the complicating herpes zoster. It was our clinical impression that the herpes zoster became disseminated and that the final event in the patient's illness was the further complication of pneumonia.

Jack L. Titus, M.D.**

Myelomatous lesions were present in the spine, ribs, and skull. Histologically, these were composed of sheets of large cells with abundant basophilic cytoplasm, large eccentrically situated nuclei with clumped chromatin and prominent nucleoli, occasional mitotic figures, and occasional binucleate and giant forms. The bone marrow in uninvolved regions was slightly hypercellular, but otherwise normal.

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*Section of Medicine, Mayo Clinic and Mayo Foundation.

**Section of Experimental and Anatomic Pathology.

Skin Lesions

Numerous hemorrhagic papules and vesicles covered the skin diffusely; in some areas they were confluent. The vesicular component of the lesion was most marked over the right lower part of the chest. The skin lesions were intraepidermal vesicles in various stages of development; most were composed of epidermal cells showing "ballooning degeneration" with eosinophilic intranuclear inclusions, proteinaceous fluid, and inflammatory cells.

The Lungs

Fibrinous pleuritis and a right pleural effusion (300 ml.) were present. The lungs were markedly edematous and congested (total weight 2020 gm.) ; they contained foci of early bronchopneumonia.

Other Findings

Multiple acute ulcers were present in the stomach, duodenum, colon, and gallbladder. The surface of some of the necrotic ulcers contained epithelial cells with intranuclear inclusions, and in some sites, numerous inflammatory cells were seen throughout the muscular wall.

In some focal areas of acute hemorrhagic pancreatitis, intranuclear inclusions were present. Tiny abscesses were observed in the adrenal cortex and the liver.

Some nerve ganglia showed perivascular cuffing with inflammatory cells, degenerative changes of ganglion cells, and severe congestion or even hemorrhage. No inflammatory lesions were found in the brain, although small capillary hemangiomas were present.

Anatomic Diagnoses

The major anatomic diagnoses were (1) multiple myeloma involving the skull, ribs, and spine, and (2) herpes zoster with visceral dissemination.

Dr. Silverstein

Dr. Martin, would you comment on herpes zoster as an infectious disease, its relationship to chickenpox in childhood, and some of the complications that the illness may produce?

William J. Martin, M.D.*

Chickenpox

Bokay, in 1893, noticed that children exposed to adults with herpes zoster might develop varicella. Morphologically, no consistent differences are seen between the changes induced in cultures of human tissues by the agent of chickenpox and that of herpes zoster. Complement-fixation, fluorescent antibody, and neutralization procedures have shown no significant antigenic differences between the two viruses.

The varicella-zoster virus is highly host-specific and has been trans-

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*Section of Medicine, Mayo Clinic and Mayo Foundation.

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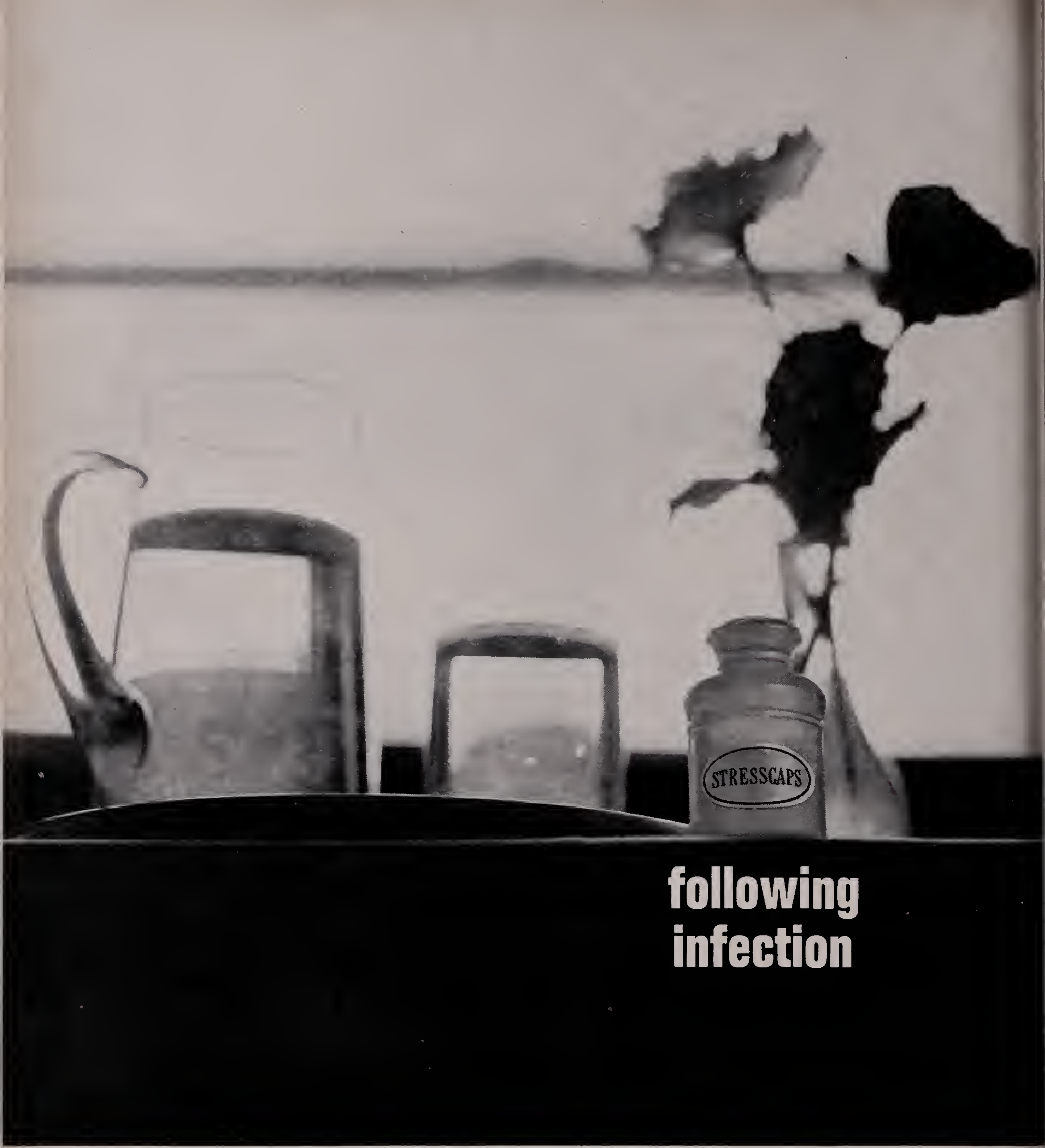

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mitted experimentally only to man. The insusceptibility of common laboratory animals to varicella-zoster virus has hampered etiologic investigations; but it provides a useful characteristic in differential diagnosis, since the viruses of herpes simplex and of variola (smallpox) may be propagated in the embryonated hen's egg and in various animals.

The majority of patients with herpes zoster give a history of a previous attack of chickenpox in childhood. Also, herpes zoster is more common in persons who are physically exhausted or who have an underlying debilitating disease. Herpes zoster following trauma such as spinal puncture, or associated with a spinal-cord tumor, lymphoma, or lymphatic leukemia, has suggested the possibility that the virus may remain dormant in the tissues for long periods of time. Since the viruses of herpes zoster and of chickenpox are similar, if not identical, it has been postulated that one virus can cause different diseases in the susceptible and partially immune subject. In other words, chickenpox may constitute the response of the nonimmune host and herpes zoster, that of the partially immune person.

Complications of Herpes Zoster

Some of the complications of herpes zoster include secondary bacterial infection of the ruptured vesicles, which is common. *When the nasociliary branch of the gasserian ganglion is involved,* the cornea, sclera, or ciliary body may be permanently damaged. Disease of *the geniculate ganglion* may lead to lesions of the concha of the ear, the external auditory canal, and the soft palate and loss of taste (Hunt's syndrome) ; this is often accompanied by paralysis of the seventh nerve. As in the case at hand, in 2 to 5 per cent of patients a generalized vesicular eruption simulating chickenpox occurs (zoster generalisatus). In such cases, dissemination generally takes place within a few days after appearance of the initial lesions, and the cutaneous involvement is often so extensive as to include the palms and soles. The *eyes, mucous membranes, and lungs* may be affected. *Headache and meningismus* are fairly frequent, and up to 50 per cent of patients have leukocytosis of the spinal fluid. A more serious complication is so-called zoster myelitis which was first described in 1876. Encephalitis or encephalomyelitis also occurs and has caused death. In these more serious cases, the cerebrospinal fluid may contain large numbers of leukocytes and high protein and low glucose concentrations. It is not known if zoster encephalomyelitis reflects direct extension of the virus or an autoimmune mechanism. Postherpetic neuralgia appears to be limited to the aged with arteriosclerosis.

Dr. Silverstein

Dr. Martin, we know that patients with myeloma have defective defense mechanisms. The proteins that these patients make have very poor quality, in regard to their effectiveness as antibodies. Would you comment regarding the role that antibodies play in viral infection in general, and would you also comment on the incidence of viral and other infections in malignant disease?

Dr. Martin

Infection with a virus is followed by the development of antibodies to the specific virus, and immunity is correlated with the continued avail-

Continued

ability of these antibodies. Yet it is not known precisely why immunity is not developed to certain viral diseases (herpes simplex) but persists indefinitely to others (mumps). Another oddity is that one cannot produce effective immunity against some viral diseases by means of inactivated viruses (smallpox) but can against others (rabies). It is important to recall that, in contradistinction to immunity, recovery from a viral disease appears not to be correlated with the development of circulating antibodies despite their concurrent appearance, since conquest by the host of the virus takes place at the cellular level.

Herpes Zoster vs. Malignant Disease

We have already noted increased incidence of herpes zoster in patients having spinal-cord tumor and in those having malignant disease, particularly lymphoma and chronic lymphatic leukemia. There are other examples of increased incidence of infectious disease in patients having neoplasia. Twenty to twenty-five per cent of patients with bacteremia due to gram-negative bacilli have underlying malignancy—such as lymphoma or a hematologic disorder—such as multiple myeloma and agranulocytosis. Repeated pneumonia, urinary-tract infection, and bacteremia show an increased incidence in patients with multiple myeloma. The incidence of cryptococcosis is increased in patients having lymphoma, and mucormycosis is fairly common in patients debilitated by malignant disease.

Since the patient at hand developed pneumonia it may be well to say a few words about this complication in victims of multiple myeloma. The increased incidence of this complication in these patients is well known, and while it may result from infection due to various micro-organisms, it is most commonly caused by pneumococci. Incidentally the prognosis in type-3 pneumococcal pneumonia is regarded as being especially guarded, in part at least, because of the frequency with which type-3 infections occur in patients having debilitating underlying diseases such as multiple myeloma. Also, the type-3 pneumococcus possesses an unusually thick capsule, is especially difficult for neutrophils to engulf, and is the pneumococcus most likely to produce pulmonary abscess. In connection with your remarks concerning defective defense mechanisms in patients with multiple myeloma, the resistance of the host to pneumococcal infection is enhanced by specific antibody which not only increases phagocytosis but also retards the spread of bacteria in the tissues. However, recovery is not entirely dependent on the immune response, since antibody is not invariably demonstrated in patients who recover with or without antibacterial therapy.

In regard to the patient under discussion, we noted previously that in cases of disseminated herpes zoster the lungs may be affected.

Dr. Silverstein

Dr. Martin, aside from prophylactic therapy in the form of vaccines, are there any viral illnesses for which effective therapy is currently or potentially available?

Dr. Martin

Treatment with Immune Serum Globulin

Gamma globulin (USP immune serum globulin) has potential use in the management of rubeola, infectious and serum hepatitis, poliomyelitis, and perhaps rubella and varicella. Use of gamma globulin has been advocated in children with leukemia, lymphoma, and those receiving immune-suppressing treatment, such as treatment with steroids or irradiation, when they get chickenpox. Gamma globulin rarely prevents chickenpox, but when administered in doses on the order of 0.6 ml. per kilogram of body weight it may modify the effects of the disease. Gamma globulin may not be totally effective in preventing hepatitis, but it affords protection in the form of reduced clinical severity of the disease for two to six months. Investigators currently are evaluating the use of gamma globulin at the time of blood transfusion as a preventive measure against serum hepatitis. Gamma globulin has been used in attempts to modify or protect against poliomyelitis, but it appears to have no protective value in preventing the disease after an individual has been exposed.

Hyperimmune Gamma Globulin for Mumps

Mumps-specific gamma globulin (hyperimmune gamma globulin) may decrease the risk of development of mumps and, given early in the disease, may reduce the incidence of complications. Use of USP immune serum globulin has no demonstrable effect on the disease.

Hyperimmune Vaccinia Gamma Globulin

Human hyperimmune vaccinia gamma globulin may prevent or modify smallpox if given within 24 hours after exposure. Passive protection may be provided after accidental exposure to vaccinia virus in a patient with extensive lesions of the skin such as eczema or burns. It also may be useful in the treatment of certain complications of vaccination such as vaccinia necrosum.

Hyperimmune Horse Serum for Rabies

An advance in antirabic therapy is the availability of hyperimmune horse serum. In persons with multiple severe bites, particularly about the head and neck, who probably have received large amounts of rabies virus, the incubation period may be so short that vaccination cannot produce immunity soon enough. Use of hyperimmune horse serum may provide passive protection until vaccination has stimulated active immunity. The patient's sensitivity to horse serum should be determined beforehand. In this regard, because of the high incidence of reaction to horse serum, a drive is under way to obtain blood from veterinarians who have had the full course of antirabies vaccine after exposure to rabies. It is hoped that serum obtained from such blood will be sufficiently effective to replace hyperimmune horse serum.

Topical Idoxuridine for Corneal Ulcers

The effectiveness of topical idoxuridine (IDU) in acute, superficial corneal ulcers appears to have been demonstrated, but its usefulness in other herpetic lesions such as those of the skin is less definite; the drug is commercially available. A drug currently under investigation is Cytosine arabinoside hydrochloride (CA), which also appears to be effective locally against herpes simplex and may be synergistic with IDU in antiherpes therapy.

Continued

Treatment for Smallpox Contacts

M-Isatin-β-Thiosemicarbazone (Methisazone), a semicarbazone derivative given orally, is effective in protecting smallpox contacts. The drug may cause nausea and vomiting, but serious toxicity in patients receiving the drug on an investigational basis has not been reported to date. In experimental animals there is some evidence of an hepatotoxic effect. *M*-Isatin-β-Thiosemicarbazone is protective regardless of the contact's vaccination status, but is ineffective once infection is established.

Influenza

1-Adamantanamine hydrochloride (Amantadine), also given by the oral route, may be useful in both preventing and treating influenza. No serious toxic effects have been reported on investigational use of the drug in patients as yet. Amantadine also may have potential use in rubella.

Paolin, a marine glycoprotein having antiviral properties, was originally isolated from the oyster, but it has also been extracted from other marine animals including the clam, sea snail, queen conch, squid, and abalone. The antiviral properties of this new antibiotic have been tested in mice and monolayer rabbit tissue cultures. In mice, a single prophylactic intraperitoneal injection of 2.5 mg. per kilogram reduced the poliovirus mortality rate almost to half of that observed in the control group.

Streptothricin, an antibiotic, is active in vitro against certain viruses causing hepatitis.

Interferon and its antiviral activity currently are the subject of considerable investigation. This natural product, one source of which is mammalian cells, appears to prevent the cells of the host from supporting viral growth, perhaps by inhibiting the cellular synthesis of viral nucleic acids. In experimental animals, viremia will stimulate production of large amounts of interferon, and foreign nucleic acids also will act as endogenous interferon producers. Production of interferon in chickens and mice has been induced by injections of live strains of *Brucella*, but not by heat-inactivated *Brucella*. Statolon, a product of *Penicillium stoloniferium*, is being investigated for its interferon-stimulating potential. As a generalization, interferon is species specific and virus nonspecific. That is to say, chicken-produced interferon fails to protect mice from viruses, and mouse-produced interferon will not inhibit viral infection in chickens. While interferon is generally species specific, there is a notable exception since simian interferon does have some degree of activity on human cells. Interferon is virus nonspecific since fresh cells are resistant not to just one virus but to many. Currently interferon is obtained from cells infected with a virus in a test tube or from experimental animals infected by injecting a virus into the blood. In the latter case, interferon produced in the animal's cells appears in the serum and is obtained by bleeding the host. A future possibility is synthesis of the substance. Theoretically, in the therapy of human diseases of viral origin, the use of nonviral substances, such as either animal or yeast nucleic acids, or of avirulent viruses might result in the continuous production of large amounts of interferon. This approach would have the advantage of eliminating the species barrier and of making the substance available prior to its possible synthesis.

In addition to the aforementioned, numerous other substances currently are being investigated for antiviral activity.

Dr. Silverstein

Dr. Martin, what possible role do you think various forms of therapy may play in the precipitation or dissemination of viral and other infections in patients with malignancy?

Dr. Martin

Again taking bacteremia due to gram-negative bacilli as an example, certain forms of therapy appear to play a role in the genesis of the infection in patients with malignancy. These forms of treatment include surgical and instrumentative procedures and intravenous injections as well as the administration of antimicrobial, antimetabolic, and adrenocorticosteroid agents; the influence of irradiation is less definite. Some of these forms of therapy may play a similar role in other infections, such as mucormycosis, and in certain viral infections as well.

In regard to viral infections, aspiration of cerebrospinal fluid appears to have precipitated herpes zoster. The incidence of herpes zoster also appears to be increased in patients treated with arsenicals.

Several deaths have been attributed to chickenpox in children who were receiving steroids because of rheumatic fever. Use of these agents has been recommended in complicated herpes zoster, but in view of these fatalities in children, steroid therapy in infections due to the varicella-zoster virus would appear to be somewhat hazardous. There is some evidence indicating that steroids may interfere with interferon production. Some investigators have concluded that treatment with adrenocorticotrophic hormone, adrenocorticosteroids, roentgen rays, and radiomimetic drugs appears to increase the possibility of dissemination of the virus in patients with localized herpes zoster.

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*Section of Experimental and Anatomic Pathology.

The Rx in Ancient Medical Manuscripts

"The symbol Rx used today as the prefix of the physician's prescription is not, as is frequently supposed, an abbreviation of a Latin word meaning recipe or compound, but is an invocation to Jupiter, a prayer for his aid to make the treatment effective. It is one of the superstitious elements that has clung to medicine even though its significance has been lost; it persists now merely as a convention."*

It is more likely, however, that the Latin *recipe* was used by the Romans, not as a noun but as the imperative form of the verbo *recipio* — to take.

Substantiation for this is supplied by Webster:

> Rx (L. Recipe.) Take.
>
> Note. — This character is reputed to have been originally the same as ♃, the symbol of Jupiter, which was placed at the top of a formula to propitiate the king of the gods, that the compound might act favorably.

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*Haggard, Howard W., M.D.: "Devils, Drugs, and Doctors."

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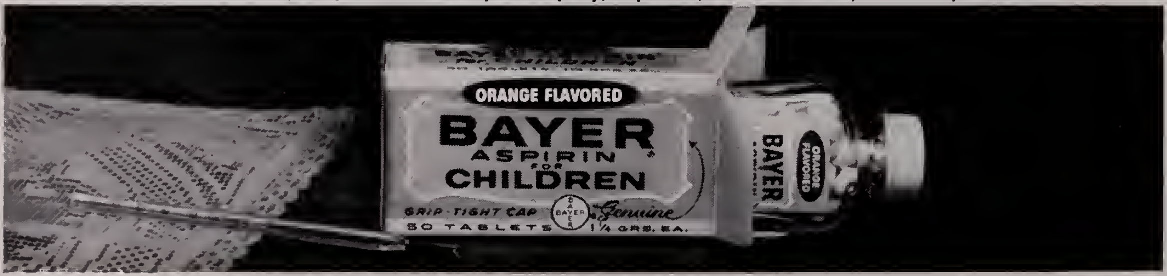
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Neuro-Pediatrics Conference

Sturge-Weber Syndrome*

Dr. Robert van Tassel:** This 12-year-old white male is a product of a normal pregnancy which was terminated by a Cesarean section for suspected RH incompatibility. He weighed seven pounds, four ounces at birth and was considered normal, except for a port-wine nevus over the right trigeminal nerve distribution. His developmental milestones in the first year of life were normal.

At 11 months of age, he became quite irritable and had a grand-mal seizure characterized by twitching of the left eye, followed by a focal left-sided convulsion which started in the left hand and arm. The diagnosis of Sturge-Weber syndrome was suspected. An electroencephalogram, pneumoencephalogram and arteriogram were performed, but were felt not to be diagnostic for this syndrome. He was then taken to the University Hospital at Ann Arbor, Michigan, where he was placed on Dilantin and Mebarol, which seemed to decrease the number of left-sided seizures.

He was admitted to the University Hospital at Ann Arbor at age 16 months, for further evaluation, at which time he was having anywhere from three to nine left-sided seizures per day. Physical examination revealed an irritable child with a port-wine nevus involving the right cheek, eye and forehead, and the right megalocornea. Also a left hemiparesis was noted. On the basis of the clinical findings a definite diagnosis of Sturge-Weber syndrome was made; and a recommendation for a right-sided hemispherectomy was rejected by the parents. Skull films taken at this time showed no calcification. The child was placed on Dilantin, Mebarol and Mesantoin, which seemed to control his seizures. The doses of these medications have been varied throughout the years depending on the number of seizures per week, most of these occurring during the day. However, the parents feel that the number of seizures is increasing. Presently the child is on Phenobarbital, 60 mg. T.I.D. and Dilantin, 100 mg. T.I.D.

He has been attending special classes since age six. The family moved

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*Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatric conferences are held the first and third Wednesdays of every month from 3:15 to 4:15 p.m. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Robert W. ten Bensel, in Pediatrics, and Dr. Robert Soll, in Adult Neurology.

**Senior medical student, University of Minnesota Medical School.

Continued

to Minneapolis in the summer of 1962, where he is now attending special classes at Warrington Elementary School.

Family history shows that both parents are living and well, and there are three other living children. The younger sister, age three, has congenital deafness and is being followed at the University Hospitals. One other child died from hydrocephalus, and one sibling was a stillborn.

Review of systems shows that he does have headaches, often preceding and following a seizure. The mother feels he has difficulty with his vision and must squint to look at things which are quite close to him. His hearing appears good; otherwise there are no particular problems.

Physical examination shows an obese child who is somewhat slow to respond. A port-wine nevus is noted in the right trigeminal area (Figure 1) as well as a small port-wine nevus in the occipital region on the right. His pupils are unequal, the right eye being larger than the left, and the fundi are difficult to examine. The left thumb is smaller than the right and there is mild impairment of two-point discrimination and simultaneous extinction on the left. However, no weakness is present on the left. The remaining physical examination is within normal limits, and no pyramidal tract signs are present.

The Evaluation

The child was referred to the University Hospitals by Dr. A. H. Wolf, Minneapolis, for: 1. Control of his seizures; 2. Prognosis and possibility for further educational training.

Mrs. Jessica Swain*

The two older children seem to be mature individuals. The mother appears to be high-strung and works from eight to 18 hours per day. The family moved to Minneapolis from Ohio two years ago in hopes of "starting over." The patient's medical problems appear not to be influencing the present difficulties at home. The family will not consider institutionalization, as they have been told that the child will not live through adolescence. No other social agencies are working with the family, as the mother has refused help from any other agencies.

Dr. Paul Moe**

In the Sturge-Weber syndrome the primary physical finding consists of a facial nevus flammeus (port-wine nevus), usually unilateral, located above and involving one eye (Figure 1). Concomitantly with the facial nevus there are brain and meningeal angiomata on the homolateral side associated with the radiographic finding of calcification (Figures 2 and 3). The cranial calcifications are characteristically "double-contoured" as a result of calcium deposits which follow the folds of the gyri. Cortical calcification is usually not discernible in the first year or two of life and has thus been confusing in making an early diagnosis by the classical radiographic findings.

Convulsions are an almost constant feature of this syndrome and usually occur during the first year of life in those with the more extensive facial nevi, and by two years in the lesser examples. As might be expected, the convulsions are usually focal in nature, involving the contralateral side of the body. The Jacksonian seizure pattern, as noted in this patient, is frequently seen and may be generalized in individual attacks or bouts of attacks. A history of paresis following seizures is unusually high among patients with Sturge-Weber syndrome, probably reflecting the abnormal cerebral vascular supply.

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*Court services.

**Pediatric neurologist, University of Minnesota Medical School.

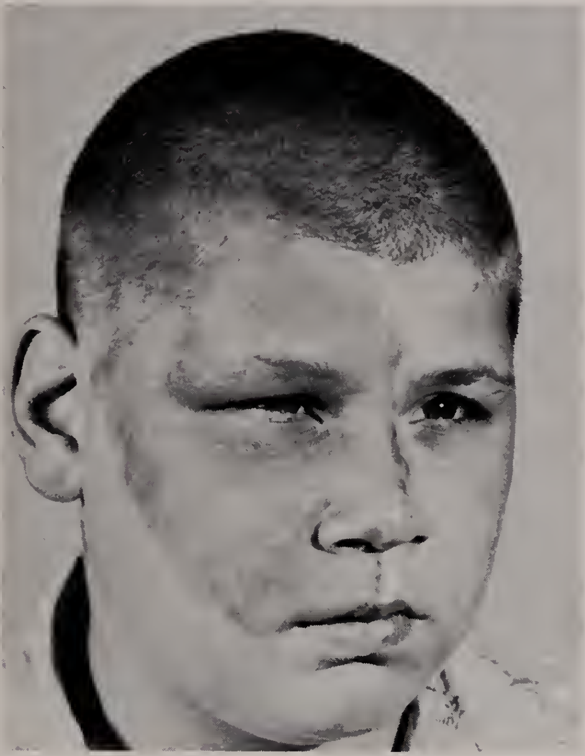

Fig. 1 — Port-wine nevus in Sturge-Weber syndrome. Note the unilateral distribution involving the eye and upper portions of the face.

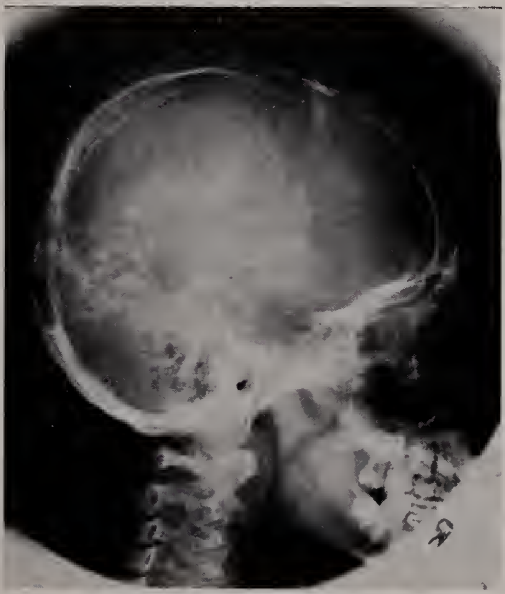

Fig. 2 — Radiograph of skull showing the characteristic "double contour" calcifications of the cortex in the Sturge-Weber syndrome. (Lateral view-right).

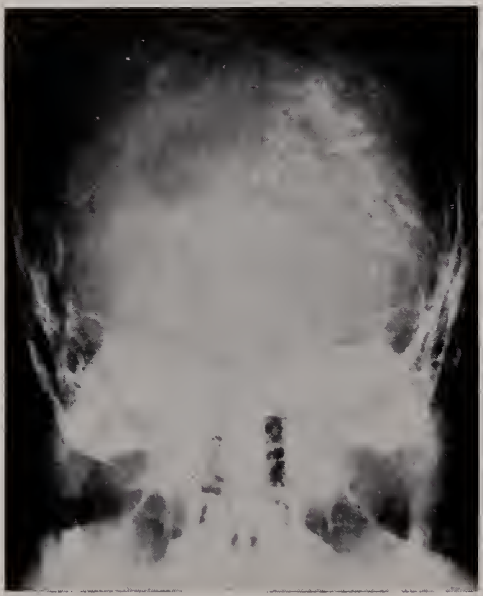

Fig. 3 — Radiograph of skull (A-P view) showing the cortical calcification of the Sturge-Weber syndrome.

Continued

Intellectual deficit is a frequently-associated symptom; the intelligence may deteriorate if convulsions are frequent. The etiology of the retardation is probably due to the abnormal meningeal blood supply on the developing cortex. Pathologically, the affected part of the brain is atrophied, and over this the leptomeninges are thick and contain a network of thin-walled vessels of the venous type. The adjacent cortex and convolutional white matter also contain an excess of similar vessels. During childhood a progressive calcification occurs within the cerebral cortex. Alexander and Norman[1] feel that this calcium deposition is a consequence of some local change in tissue metabolism conditioned in part by the presence of the overlying angiomatosis.

Therapy has been difficult in these patients, particularly in regard to seizure control. Some authors[1] feel surgical intervention with removal of pathological tissue (hemispherectomy) should be performed within two months after birth. A follow-up of 35 patients at the Mayo Clinic[2] reveals that one half of their patients are well with very few seizures. Ten patients are poorly controlled and four have died.

One seizure every three weeks represents good control. The patient should be followed at monthly intervals to regulate his medications.

Dr. ten Bensel

Genetically no familial incidence has been established, and there is equal sex distribution. A recent chromosomal abnormality has been reported, but has not been verified by others.[3,4]

Dr. Ellingson*

Examination of the eye revealed that the patient could see fingers at only two feet. Vision in the left eye appeared normal. On slit-lamp examination of the right eye, dilated vessels were noted in the region on the ciliary body but could not be definitely seen on the conventional funduscopic examination. There was Grade IV cupping present, as seen in glaucoma. The pressure in the right eye was 48 mm. of mercury (normal 20 mm. of mercury or less). This type of glaucoma is considered an open angle glaucoma, and it is not known whether this is due to venous congestion caused by angioma of the choroid or to increased production of fluid within the eye. At the present time therapy should be gauged to prevent a painful eye and to prevent a totally blind one. The child is now on Pilocarpine and an epinepherine derivative to decrease production of fluid within the eye. For the remainder of his life he will have to be on this medication, given four times a day. At present, he is administering his own medication.

Miss Joan Pabst**

The patient was a co-operative, affable child. Poor motor co-ordination and a short attention span were noted, but there was no difficulty in communicating with him. A Stanford-Binet test was performed which showed a mental age of six years and six months for an I.Q. of 58, representing four to six years retardation. It was noted that he had poor facility with numbers but did show some facility in verbal ability and in making judgments in life-situation questions. A Bender-Gestalt test showed significant signs of severe perceptual motor disturbance with evidence of organic dysfunction. However, he was considered to be educable by present standards. There had been no significant deterioration since his last I.Q. test, given in 1962.

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*Ophthalmologist, University of Minnesota Medical School.

**Clinical psychologist, University of Minnesota Medical School.

Dr. Wentworth Quast*

The child should be gauged also by the level he was functioning at in school, which appeared to be quite low. A school such as Cambridge State School would be optimal in terms of educational opportunity. In this type of situation, if the seizures could be managed and the child placed in a one-to-one relationship with a teacher, he might benefit greatly.

Dr. Frank Lassman**

The child was co-operative but was observed to have a low frustration level and a feeling of hostility. Hearing tests were all normal. Filtered speech, which tests the anterior temporal lobe, was normal. The child could repeat four numbers forward but none backwards. On a verbal-picture test he scored nine years; six months on the Nashville Norms. His visual discrimination was felt to be good, but he had great difficulty with visual memory as well as with motor co-ordination. He had no reading ability, and could not spell his name. He is felt to be educable, particularly in a one-to-one situation.

Dr. ten Bensel

There is concern about the feelings of the mother toward the child; whether or not she has a psychological need to keep the patient at home with her. Secondly, in regard to the school's work with the patient, it is questionable whether they can progress any further with him in the present situation. In view of past refusal to accept counseling from various sources, however, it was felt that another attempt should be made.

Final Recommendations

The primary aim for this patient is counseling for the parents and adequate seizure control. The parents should be advised as to his prognosis, which at the present time appears good, as he has not showed any signs of deteriorating. It is hoped that with better regulation of his seizures further educational attempts may be more successful. However, it is pointed out that control of seizures may not necessarily change matters appreciably in this regard.

The parents should be instructed to contact Hennepin County Child Service Division for counsel in regard to possible institutionalization. Under such a program the child would be awarded state guardianship as a mentally retarded child and placed on a waiting list (which is usually two to three years) for possible institutionalization. If the school is at the end of its educational efforts and is performing only custodial care, and if the mother refuses further consultative help, it is planned to make a recommendation through Court Services, instructing that since other efforts have failed, optimum educational opportunities can be afforded through institutionalization at Cambridge. It is hoped this last step will not have to be resorted to as the other measures should be tried first.

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*Clinical psychologist, University of Minnesota Medical School.
**Audiology department, University of Minnesota Medical School.

Continued

Those participating in the conference include: Dr. Robert van Tassel, Senior Medical Student; Mrs. Jessica Swain, Court Services; Mrs. Evelyn Walman, School Social Worker; Dr. Paul Moe, Pediatric Neurologist; Dr. Ellingson, Ophthalmologist; Dr. Wentworth Quast, Clinical Psychologist; Dr. Frank Lassman, Audiology Department; Miss Joan Pabst, Clinical Psychologist; Dr. Robert ten Bensel, Moderator.

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Medical Ethics

Many people overlook one very extraordinary aspect of medical ethics. You see, medicine originated in religion, and as a profession it has retained in its principles some of the religious virtues of self-sacrifice to the suffering of others.

It follows a course that must seem most impracticable to many men of commerce. It is this: A man may invent a mechanical device for the comfort, profit, or pleasure of mankind; manufacture and sell it to his financial betterment, keeping his process secret or protected by patents. He can do all this quite honorably; even if he becomes rich, no one looks at him askance — indeed, quite the reverse. Such is not the case in medicine.

A physician or dentist who seeks and finds a means of alleviating suffering or prolonging life makes his discovery public that all may see and benefit without financial recompense to him. Such a procedure is followed in no other branch of human learning practiced for a livelihood. This obligation which the physician and dentist accept, and enforce, is looked upon as a natural course by all of those people who accept as equally natural quite the opposite course from all other members of society.

Haggard, Howard W., M.D.: The Lame, the Halt, and the Blind. Harper & Brothers, New York and London, 1932.

Democracy is a method of our getting ahead without leaving any of us behind.
—T. V. Smith

Efficiency expert: One who is smart enough to tell you how to run your business and too smart to start one of his own.—Anonymous

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More people die of success than of cancer.— Rabbi Heschel

Infections of the Urinary Tract

Part I — Some Nosologic and Etiologic Considerations

WILLIAM J. MARTIN, M.D.*
RICHARD D. WAGONER, M.D.*
Rochester, Minnesota

IN THE preceding two decades, advances have been made in the ability to diagnose and treat infections of the urinary tract. Consequently, the physician has available a more accurate and satisfying approach to the individual problem at hand. Although not all infections are amenable to therapy, treatment can prevent further deterioration of renal function in many cases and alleviate symptoms in most cases. Prevention of significant renal injury consequent to infections of the urinary tract remains the primary goal of the physician; early detection of infection, along with judicious management, makes his goal progressively achievable. It is commonly accepted that infections of the urinary tract are second in incidence only to respiratory infections.

Infections of the urinary tract are difficult to discuss since they have varied pathogenesis, symptomatology, and prognosis; consequently an extensive terminology based on various etiologic and clinical nuances has accrued. There are such nosologic entities as septic infarct, renal carbuncle, perinephritic abscess, primary versus secondary infection, ascending versus descending infection, and pyelitis versus pyelonephritis. Whatever the name, the basic disease is infection; the same infecting organisms are common to the various syndromes; and the essential purpose of diagnosis and treatment is eradication of the infection.

For present purposes, this extensive terminology will be avoided, and instead infections of the urinary tract will be discussed from the point of view of the following clinical syndromes.

Clinical Syndromes

Asymptomatic Bacteriuria

While known to be of increased incidence in certain conditions, asymptomatic bacteriuria also seems to occur in persons who otherwise appear to be normal. If infection of the urinary tract is manifested by asymptomatic bacteriuria and can be detected and eliminated, some cases of ultimate renal insufficiency might be avoided. Persons who have asymptomatic bacteriuria may contribute to the discrepancy between clinically recognized infection of the urinary tract and its higher incidence at necropsy. In this regard, chronic inflammatory interstitial lesions of the renal parenchyma (labeled pyelonephritis) may represent processes other than primary bacterial infections, such as those due to various toxic chemical agents, metabolic abnormalities, and vascular changes. A critical question is whether asymptomatic bacteriuria usually leads to

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*Section of Medicine, Mayo Clinic and Mayo Foundation.

pyelonephritis or whether pyelonephritis usually arises because previously damaged kidneys become infected, with resultant bacteriuria.[1] In our present state of knowledge, it appears wiser to conclude that urinary infection including renal involvement does or is likely to occur[2] in patients having persistent bacteriuria of significant degree.

Infections

Acute infections of the urinary tract vary considerably in pathology and symptomatology. At one end of the gamut there occurs the so-called simple infection, which commonly is seen in young or middle-aged women. Often it is not associated with detectable underlying uropathy and, being intrinsically a self-limited disease, may respond to minimal medical management. On the other end, there is included such serious states as renal abscess, which may be associated with bacteremia or endocarditis. In most acute infections of the urinary tract, local and constitutional manifestations parallel the degree of urinary infection, but occasionally they may not.

Recurrent infection of the urinary tract often develops in the absence of underlying uropathy or predisposing disease, but such infection should always be excluded by careful urologic and microbiologic investigation. The physician also should attempt to distinguish such recurrent infection from chronic infection in exacerbation, although occasionally the distinction is difficult if not impossible. Recurrences probably reflect reinfection, relapse, and superinfection in decreasing order of incidence.

In chronic infection of the urinary tract, unlike acute simple and recurrent infections, underlying uropathy often is present. The underlying obstructive lesions of the urinary tract may be structural or functional and either acquired or congenital. Such obstruction, with poor drainage of urine, may be attended by varying degrees of dilation of the bladder with trabeculation and hypertrophy, hydroureter, and hydronephrosis. A considerable number of chronic infections are relatively asymptomatic, and some of them may present as asymptomatic bacteriuria. Flare-ups of smoldering and active, but silent, infections may occur, especially in the presence of undetected incomplete urinary obstruction. In contradistinction to the acute process wherein there usually are local and systemic manifestations of infection, the principal findings in chronic disease are likely to be those related to previously sustained renal injury. These latter findings may include proteinuria, abnormal urinary sediment, azotemia, and calyceal changes on excretory urography. Chronic urinary infection is often of insidious onset, since frequently at the diagnosis no history of urinary infection in earlier life may be obtained.[3] Also, patients known to have had multiple attacks of acute infections may not show progression to chronic disease even after many years. Thus, preceding acute urinary infection and chronic pyelonephritis perhaps are not a necessary sequence. However, until more complete data are available, the best empiric approach to the problem probably is tentative acceptance that the earlier and more completely the acute infection is eradicated, the better is the ultimate renal prognosis. Lack of previous diagnosis does not necessarily exclude occurrence; perhaps prior infection presented as an unexplained fever in earlier life.

Etiologic Factors

Uropathogenic Bacteria

In the causation of the infections of the urinary tract, the first necessity obviously is an uropathogenic strain of bacteria. The five most frequently causative ones are (1) coli-aerogenes organisms, (2) Proteus organisms, (3) Pseudomonas organisms, (4) streptococci, usually enterococci, and (5) staphylococci.

Bacterial Source

The theory that most cases of urinary infection reflect entry of bacteria into the tract via the urethra and the subsequent ascent of the organisms to the kidney is being increasingly propounded. The bacteria appear to originate usually in the host's own intestinal tract, except for some strains of Pseudomonas and Staphylococcus, which may be of exogenous origin.

Vesicoureteral Reflux

Theoretically, vesicoureteral reflux on micturition would abet infection of the kidney by the ascending route. Such reflux may be a constitutional characteristic in some individuals but appears to be lacking in most normal persons. Some investigators[4] have said that acute cystitis may produce temporary ureteral reflux and that repeated infections may produce persistent reflux. Thus, actualization of a vicious circle is theoretically possible, wherein recurrent infection may destroy ureterovesical continence and permit consistent hydrostatic injections of infected urine into the kidneys until chronic pyelonephritis is established.[4]

Age and Sex

Infection of the urinary tract is a disease of children of both sexes, women of the child-bearing age, and the elderly of both sexes. It is seldom seen in adult men in middle life. The frequency of urinary obstruction on either a congenital or an acquired basis and the ease of entry of bacteria into the urinary tract are the chief factors in these differences of age and sex. Overt infections of the urinary tract are three times more common in women than in men. Asymptomatic bacteriuria also is more common in females than in males. About two thirds of these infections in women occur before they are 40 years old, and two thirds of those in men occur after they are 40 years old. Despite the higher clinical incidence of infections in women, the disease may be comparatively more lethal in men, as evidenced by the fact that, at necropsy, it is almost equally frequent in the two sexes.

Underlying Uropathy

Numerous structural abnormalities[5] along the urinary tract, such as urolithiasis, strictures, cysts, and tumors, may produce stagnation and consequent infection. Until disproved, the probability of prostatism in men more than 50 years of age who have urinary infection is high. The external genitalia of men should be examined for such abnormalities as pinpoint meatus and phimosis, while women should be examined for pelvic relaxation, infiltration of the bladder by carcinoma, and the like. Underlying uropathy that is most commonly susceptible to surgical correction is found in the very young and in men more than 40 years old. Adequate removal of demonstrated obstructions may bring about cure of infections per se.

Pregnancy

In pregnant women, urinary infections are at least twice as frequent as in nonpregnant women; except for excessive gain in weight, pyelonephritis probably is the most common complication of pregnancy. The flow of urine is slowed by the dilated and distorted ureters, made atonic by the increased secretion of progesterone, and subjected to the pressure of the enlarging uterus; in the last trimester the bladder becomes compressed, resulting in further urinary stasis. Infection is particularly frequent in the last trimester and is common in the puerperium. It is striking that the right side is much more frequently affected than the left in the gravid state. Infection may be more common in negro women than white women. Further, urinary infections are said to be almost twice as common in toxemic as in normal pregnant women.[6] In pregnant women, asymptomatic bacteriuria may occur weeks before frank symptoms of urinary infection, and pyelonephritis of pregnancy probably occurs almost exclusively in women with pre-existing bacteriuria. Approximately 4 per cent of gravid women have bacteriuria, and of this group about one in five develops acute pyelonephritis if left untreated. Kass[7] has found that 0.5 gm. of sulfonamide given daily for one to two weeks during the period of asymptomatic bacteriuria usually prevents acute pyelonephritis in these women. Of pregnant women with bacteriuria, only one third have urinary symptoms; however, symptoms are noted in about half of those with previous episodes, in contrast to only one fourth of those without earlier complaints.[8]

Urethral Manipulation

Infection of the urinary tract follows single catheterization in 2 to 4 per cent of patients, and it develops in almost all pa-

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tients who have indwelling catheters for several days, whether or not antibacterial prophylaxis with chemotherapeutic or antibiotic agents administered systemically is given. A possible exception to this latter generalization is when the catheter can be removed in 72 hours; in such cases systemic antibacterial prophylaxis may be beneficial. In patients requiring prolonged use of a catheter, 0.1 per cent solution of lactic or acetic acid delivered via slow drip into the bladder by an indwelling catheter may reduce the pH of the urine to 5 or less and thereby prevent infection. However, the procedure is somewhat cumbersome, and urine must be released every two hours. Irrigation of the bladder several times daily with chlorhexidine (1:20,000) also has been recommended in patients with indwelling catheters. Continuous use of a neomycin-polymyxin B rinse via a three-way catheter may be even more efficacious in preventing infection and especially in forestalling bacterial invasion of the blood.[9] The three-way instrument has an extra lumen — an inflow tube added to the usual outflow and balloon lumens. The inflow is used to introduce, during 24 hours, a very slow drip of saline (1000 ml.) to which has been added 40 mg. of neomycin and 20 mg. of polymyxin B. Attempts at prolonged systemic antibacterial prophylaxis with agents such as the sulfonamides may serve only to eliminate more susceptible organisms and consequently predispose to infection with enterococci and Proteus, and Pseudomonas organisms which ultimately require more heroic therapy.

Manipulation, including catheterization, of an infected urinary tract may result in bacteremia and sometimes fatal bacteremic shock, if treatment is not given beforehand to control the infection. While this premanipulative antimicrobial therapy may control the infection to the point of disallowing bacterial invasion of the blood, such therapy usually will not eradicate the infection, especially when there is underlying uropathy. If fever occurs after urologic manipulation, both the urine and the blood should be cultured.

The risk of infection from catheterization or other urethral instrumentation varies with the individual situation and the reason for catheterization; but, no matter how carefully executed, these procedures carry the inherent hazard of iatrogenic bacterial contamination and infection. In every case, there is the potential that pathogenic bacteria in the urethra can be pushed into the bladder with the tip of the catheter or instrument. In addition to contaminating the urine specimen obtained, one may, if residual urine is present or if the patient has diabetes, infect the remaining urine and increase the likelihood of postcatheterization urinary infection. Organisms virtually always are recoverable from the distal centimeter of the male urethra and from about half of male urethras at a depth of 5 cm. In women, organisms are recoverable at a depth of 2 cm. from most urethras. Normal urinary tracts have considerable resistance to infection, so that instruments may be used in them with relative impunity, and consequently catheterization of normal persons seldom causes infection. However, this may have less than major application to the problem, since manipulation is more likely to be carried out in persons who do not have a normal urinary tract. Little dispute appears regarding the increases in danger of postcatheterization infection by pre-existing disease of the urinary tract. Regardless of whether the catheter introduces infection, continued use of the instrument in selected situations is unavoidable. Such use has relieved many patients of painfully distended bladders and has saved some from uremic death. The problem is not whether the catheter should be used but rather how it can be used more efficiently. The implication is obvious, however, that adequate attention should be paid to the technic of catheterization and that the catheter should be used with discrimination.

Antibacterial-Induced Floral Changes

In general, antibacterial agents may be responsible for iatrogenic changes in the body flora, resulting in urinary infections; for example, penicillin and allied drugs, perhaps given for a respiratory infection, may depress the gram-positive elements, and the overgrowing gram-negative bacteria may invade the urinary tract. Conversely, drugs depressing the gram-negative flora, such as the tetracyclines, may allow overgrowth of gram-positive bacteria and consequently urinary invasion.

Predisposing Disease

Certain diseases, such as diabetes mellitus, predispose to infections of the urinary tract. Some diseases, such as hyperparathyroidism and lymphoma, may predispose to infection by inducing obstructive uropathy. Others, such as amyloidosis and glomerulonephritis, may be complicated by secondary infection. The sickling trait may result in vascular thrombosis and changes in the renal medulla which may enhance infection.

Metastatic Infection

Metastatic involvement of the kidneys, as exemplified by septic infarcts in bacteremia or endocarditis, is an obvious factor. There is the paradox that, conversely, septic emboli may arise from the kidney and produce metastatic abscesses elsewhere.[10] A furuncle or carbuncle that is present a few weeks before the onset of a perinephritic abscess is suggestive of a staphylococcal cause.

Miscellaneous

Nonspecific antibacterial substances have been described as being present in normal urine; their disappearance or the appearance of other substances encouraging bacterial growth in the urine are possible etiologic factors. The fourth component of complement is inactivated by ammonia, and the production of ammonia from glutamine by the renal medulla has been given in explanation of its special susceptibility to infection. However, the current concept is that low complement per se does not predispose to infection elsewhere in the body. Some evidence exists that the mucosal cells of the urinary bladder possess an antibacterial mechanism that may explain spontaneous subsidence of certain cases of cystitis.

Trauma to the kidneys, as may occur in participants in contact sports and in victims of auto accidents, with resulting scarring, theoretically could enhance future infection.

Some investigators mention increased functional demands on the kidneys as enhancing infections. By this is meant that the burdens of drug excretion, as with some of the barbiturates, or that the excretion of metabolites, as urea after violent exercise, may exhaust the organs' resistance to the point of increasing their susceptibility to infection.

Some data have been interpreted as indicating that hypokalemic nephropathy increases the patient's susceptibility to pyelonephritis.

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All looks yellow to the jaundiced eye.—Alexander Pope

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Diabetic Nephropathy*

Diabetic "nephropathy" refers to the complex picture of arterial, arteriolar, glomerular and tubular lesions, pyelonephritis and papillary necrosis, which appear to be the inevitable consequence of long-continued diabetes.[1,2] From the time of Richard Bright it had been recognized that "nephritis" was very common in patients with diabetes, and renal tubular lesions had been described by Armanni as early as 1875. For many years these were regarded as the most valuable post-mortem evidence of diabetes. In 1936 Kimmelstiel and Wilson[3] observed and described in eight patients (seven of whom had diabetes) the unique nodular glomerulosclerotic lesion of "intercapillary" origin. Later Bell[4] and others[5] defined a "diffuse glomerulosclerosis" which was also attributed to the diabetic process. However, diffuse glomerulosclerosis was observed in other conditions and its exact relationship to nodular diabetic glomerulosclerosis remained obscure prior to electronmicroscopy. A third group of glomerular lesions, the "exudative lesions," were observed by light microscopy.[6,7] These lesions were also found in conditions other than diabetes.

"Kimmelstiel-Wilson disease or syndrome" is a misnomer arising from reference to the nephrotic syndrome and not the significant renal lesions. Diagnosing nodular glomerulosclerosis at the bedside should be avoided, and the term "Kimmelstiel-Wilson syndrome" might well be abandoned. Less than 10 percent of patients with nodular glomerulosclerosis also have the nephrotic syndrome. Diffuse glomerulosclerosis is closely associated with renal failure and proteinuria and its clinical features in diabetes.[1]

Histology, Pathogenesis, and Etiology

The lesions generally considered indicative of diabetes are: glycogen-filled epithelial cells in the straight distal portion of proximal convoluted tubules (Armanni-Ebstein cells) and nodular glomerulosclerosis.[2] Kark and Gellman have studied the diabetic kidney by renal biopsy during life and at autopsy. Kark prefers the term nodular glomerulosclerosis rather than

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*Medical Grand Rounds, Mt. Sinai Hospital, March 10, 1964.

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intercapillary glomerulosclerosis. Three types of glomerulosclerosis are recognized and described: nodular, diffuse, and exudative.

Nodular Glomerulosclerosis

Histologically this lesion is characterized by a unique nodular deposit at the periphery of the glomerular capillary tuft. The nodules appear laminated and are surrounded by one or more layers of crowded, somewhat pyknotic nuclei. In the early stages, dilated blood-filled capillaries surround the nodule. Reticulin fibers can be demonstrated in the nodules, which also contain muco-polysaccharide, lipid, and hemoglobin.[8] With light microscopy, during the earliest stage, the glomeruli are normal in size, and most of the capillaries retain normal thin basement membranes. The pertinent finding is the prominence of axial stalks due to slight widening, with deeply eosinophilic and PAS-positive deposits.[9] Occasionally there is an increase in nuclei of the mesangium. The basement membrane, as it reflects over the mesangium into the next capillary loop, is thickened two or three-fold and wrinkled. In this area there is deposition of PAS-positive filaments or fragments, which become coarse and coalesce to become small hyaline, homogenous deposits. At this stage, however, the changes are not sufficiently distinctive to warrant the designation of "nodule."

The most remarkable change by electronmicroscopy is seen in the mesangium, which widens with a conspicuously increased deposition of hyaline or basement membrane-like material not seen in normal kidneys or in diffuse-type glomerulosclerosis. Bowman's capsule is focally thickened and contains osmophilic, electron-dense, homogeneous material similar to that in the hilar vessels and preglomerular arterioles. In some areas this replaces smooth muscle cells. There is also an increase of collagen fibrils in the connective tissue surrounding the basement membrane of Bowman's capsule.

As the lesions progress, the deposit of hyaline material in the mesangium increases, and the masses become larger and coalesce. The basement membrane of many peripheral capillaries remains thin or only slightly thickened, but some areas become thickened three to five times. In these areas the epithelial foot processes become flattened and fixed, whereas the podocytes elsewhere are normal. In the advanced stage with fully developed nodules the peripheral capillaries become increasingly involved, with thickening of the basement membrane and narrowing of the lumen. There is also thickening of the tubular basement membrane and the hilar vessels. There are varying sized hyaline nodules of the basement membrane of hilar vessels protruding into their lumina.

Diffuse Glomerulosclerosis

In the earlier stage of diffuse glomerulosclerosis the basement membrane is characteristically thickened throughout the entire glomerulus and involves the peripheral portions of capillary loops. In later stages, the homogeneous basement membrane becomes much thicker, as much as ten times that of normal membrane, and is more wrinkled and folded. In addition, the basement membrane-like material in the mesangium increases greatly in amount and, together with the peripheral basement membrane, encroaches upon the capillary lumen which appears as a narrowed channel.

Exudative Glomerulosclerosis

This type is not so common or specific for diabetes as the above lesions. The long-standing hyperlipemia often present in diabetes may result in the development of fat globules in the tubules or in the glomeruli.[8] The tubular changes described in 1875 by Armanni-Ebstein as hyaline drops and vacuolation in the kidneys have now been shown to contain glycogen. Histochemically they stain as fibrinoid. The deposits have been shown to contain gamma globulin and frequently some lipid.[10] This type of change is not seen in renal biopsy specimens and is even infrequently seen at autopsy, since treatment of diabetes has improved.

In prediabetic adults, similar changes have been described by various authors. In a study performed on 11 diabetic and two prediabetic children, glomerular lesions were observed by electron microscopy even in the absence of renal dysfunction, hypertension, or retinopathy.[11] This nephropathy was focal within glomeruli and was characterized by accumulation of basement membrane-like material in mesangial areas, thickening of the basement membranes of capillaries, and electron-dense "deposits" randomly distributed in these regions. No relationship was demonstrable between nephropathy and the age of the patient, the duration of illness, the dosage of insulin, or the degree of diabetic control. The most significant change was a minimal increase of PAS-positive material in mesangial areas, which apparently represents the earliest manifestation of diabetic and prediabetic nephropathy detectable by light microscopy.

Two possible explanations are suggested by these findings. (1) The nodular form of diabetic glomerulosclerosis develops from the diffuse lesion by enlargement of hyaline deposits, which differ from each other only in the size and shape of the mass. (2) The specific nodule originates in the mesangium (previously referred to as intercapillary space) with secondary involvement of the peripheral basement membrane.

Most investigators agree that diffuse diabetic glomerulosclerosis is more common than the nodular type, but that the lesion is less specific. With light microscopy, the predominant deposition of "hyaline" material in the stalk is a distinguishing feature. The deposition of basement membrane-like material in the mesangium prior to the formation of a nodule is by itself not pathognomonic of diabetes but occurs to some extent in normal glomeruli and also in a variety of other pathologic conditions.[9]

Bell[4] has stated that the diffuse glomerular lesions are much more apt to produce renal failure than the nodular ones. Kark and associates[1] confirmed this opinion by means of renal biopsies in patients with long-standing diabetes and evidence of renal involvement. They found that the increase in severity of the diffuse lesion paralleled the clinical and laboratory signs of renal failure, such as albuminuria, edema, azotemia, decreased serum albumin, and decreased creatinine and urea clearances. There was no similar correlation between the severity of nodular lesions and the evidences of advance of renal failure.[3]

With the onset of proteinuria, the capillary wall through which the proteins must pass is widened by: (1) increase in amount of endothelial cytoplasm and disappearances of the pores, (2) the greater thickness of the basement membrane, (3) coalescence of epithelial foot processes so that the entire external surface of the capillary basement membrane is

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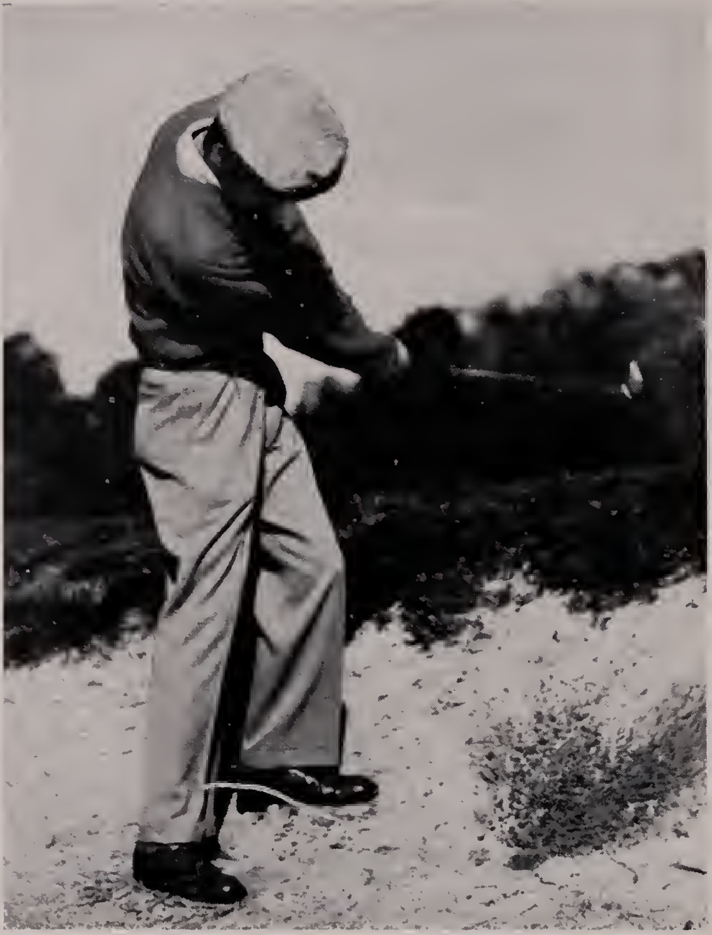

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covered with epithelial cell cytoplasm.[10] In addition, both spithelial and endothelial cells show larger numbers of mitochondria and greater amounts of endoplasmic reticulum, changes usually associated with increased cellular work and synthesis of proteins. Finally, the surface of the epithelial cell exposed to Bowman's space is extended greatly by the formation of many more canaliculi.

Almost all patients with advanced glomerulosclerosis have hypertension and severe generalized arteriolar sclerosis involving both afferent and efferent arterioles of the glomerulus. Efferent arteriolar sclerosis, as emphasized by Bell, is specific for diabetes mellitus.[4] Ischemic obsolescence of the diabetic glomeruli is quite frequent, and this process often protects the glomerulus from formation of the nodules of diabetic glomerulosclerosis.[10]

Several interesting observations have suggested a possible etiology for the glomerulosclerosis. The staining characteristics and immunochemistry of the glomerular lesions suggest an immunologic mechanism.[12] These lesions were rarely observed in autopsies on diabetic patients who died before 1923, and who had not received insulin. In addition, fewer glomerular lesions have been reported in patients who had not received insulin. Insulin binding has been demonstrated in the lesions of the diabetic glomerulosclerotic kidney but not in the lesions of nondiabetic renal diseases such as chronic glomerulonephritis and malignant nephrosclerosis. Although these observations suggest that insulin, particularly exogenous insulin, may act as an antigen and participate in the formation of glomerulosclerosis, they do not explain the fact that early basement membrane changes can be seen coincident with the clinical onset of the disease. Submicroscopic basement membrane thickening may be an invariable part of diabetes, but microscopic or clinically evident glomerulosclerosis may be the result of antigenic activity plus other unknown factors.[13]

There is no incontrovertible evidence that the specific renal lesions of diabetes can be prevented by strict control of the disease. A lower incidence of all complications is found in patients who have been well controlled than in those who have been poorly controlled. Even in the well controlled group, however, incidence of complications is high in patients followed long enough.

Symptoms, Signs and Diagnosis

There are no specific symptoms of renal involvement in diabetes.[1] In known diabetics the urine should be examined frequently for evidence of renal damage. Persistent proteinuria, white cells or casts in the absence of infection suggest that the diffuse lesion is well established. The presence of oval fat bodies and fatty casts indicates the development of severe tubular changes. Unfortunately none of these urinary findings are pathognomonic of diabetic glomerulosclerosis. The only certain method of diagnosis ante mortem is by renal biopsy; however, suspicion should be aroused by the finding of proteinuria, hypertension, and azotemia. The presence of the nephrotic syndrome makes the diagnosis virtually certain. Kark and his co-workers have presented the most comprehensive account of the clinical correlations and renal functional changes associated with diabetic glomerulosclerosis. These findings are summarized in the following tables.

Continued

TABLE 1
Clinical Features in Diabetic Glomerulosclerosis*

	Type of Pathologic Change	
Clinical Features	Predominantly Diffuse	Predominantly Nodular
Sex	No correlation	Same
Age	More severe with younger age at onset	Same
Duration of diabetes	More severe with increased duration	Same
Incidence of hypertension	Positive correlation	No correlation
Type or duration of insulin therapy	No correlation	No correlation
History of diabetic ketosis	Positive correlation	No correlation
Retinopathy	Positive correlation	Positive correlation
Peripheral vascular disease	No correlation	No correlation
Edema	Positive correlation	No correlation
Nephrotic syndrome	Positive correlation	No correlation

Positive correlation: The presence or the frequency of the clinical feature is related to increasing severity of the specific pathologic change.

No correlation: Clinical features are independent of the pathologic change.

TABLE 2
Laboratory Findings in Diabetic Glomerulosclerosis*[9]

	Type of Pathologic Change	
Laboratory Findings	Predominantly Diffuse	Predominantly Nodular
Urine		
(1) Proteinuria	Positive correlation	± Correlation
(2) Sediment—WBC, RBC, Casts	Positive correlation	± Correlation
Blood Chemistry		
(1) BUN-NPH	Positive correlation	No correlation
(2) Creatinine	Positive correlation	No correlation
(3) Serum albumin	Positive correlation	No correlation
(4) Serum cholesterol	No correlation	No correlation
Renal Function		
Urea clearance	Positive correlation	No correlation
Creatinine clearance	Positive correlation	No correlation

Positive correlation: A greater degree of abnormality of the laboratory finding is usually associated with an increasingly severe pathologic change.

No correlation: No predictable relationship between the laboratory abnormality and the extent of the pathologic change.

*Lee, Charles T., Jr., M.D.: Renal Disease in Diabetes Mellitus. Med Clin N Amer 47:1076, 1963.

The lesions show no predilection for either sex. They are more frequent and severe in patients with the lowest age of onset and with increasing duration of diabetes. Hypertension and edema are more frequently attributed to congestive heart failure than to the nephrotic syndrome. Insulin therapy cannot be correlated with the degree of pathologic change. If one uses the frequency of diabetic ketosis as a rough guide to the adequacy of diabetic control, it appears that poor control may result in proportionately more severe diffuse changes. Retinopathy and glomerulosclerosis are almost invariably found together, and the severity of one mirrors the severity of the other. For practical purposes it appears that the best and easiest way to judge the amount of renal damage in a given patient is a careful funduscopic examination. Rather surprisingly, other evidence of vascular disease in the heart, brain, or extremities bears no direct relation to the specific pathologic entity of glomerulosclerosis. On the other hand, peripheral arteriosclerosis is associated with nephrosclerosis, proliferative arterial changes, and renal artery arteriosclerosis in diabetic patients.[13]

Occasionally patients, not previously known to have diabetes, present with renal failure and glycosuria and are subsequently found to have the glomerular lesions specific for diabetes. The development of renal disease in diabetes is sometimes associated with the reduction or disappearance of glycosuria,[1] the mechanism for which is not clear. Reduction of glomerular filtration might permit the tubules to reabsorb all the glucose that reaches them. There have been occasional cases reported in which the diabetes, as measured by glucose tolerance, seemed to undergo a complete remission.[14] One factor may be the decrease in caloric intake associated with the inactivity, anorexia, and nausea of renal failure. Since a proportion of the circulating insulin exists in the body bound to serum albumin as a metabolically inactive complex, hypoalbuminemia may lead to a greater amount of free, active insulin. Finally, the immune mechanisms which produce insulin antibodies and insulin resistance may be decreased by the renal failure, and more insulin may thus become available for metabolic activity.

Prevention and Treatment of Diabetic Glomerulosclerosis

There is a definite difference of opinion regarding the prevention of glomerulosclerosis. One group believes that clinical nephropathy is inevitable in every diabetic if he survives long enough. Another group points out that patients with the most severe diabetes and with the poorest control are the ones who generally develop rapidly progressive renal failure. The question then arises: if this is an inevitable part of the severe diabetic state, why is it that occasional patients who have had the juvenile type of the disease 25 years or more do not show clinical or laboratory evidence of glomerulosclerosis? Both groups are probably partly right, since submicroscopic basement membrane changes may be present in all diabetics, but the rapidity with which these changes advance may be partially dependent upon the care exercised by the patient and physician in the control of the disease. It would still appear to be a reasonable concept that proper control of diabetes may help reduce glomerulosclerosis in the sense of helping to arrest progression.

Treatment consists of two phases: (1) control of the diabetes, and (2) management of progressive renal failure. Patients may become increasingly sensitive to insulin as the renal disease progresses and therefore may need less and less insulin. Since the high renal threshold gives a false impression of improved control of hyperglycemia, more reliance must be placed on the blood sugar as the index of diabetic control.[13] Once severe renal involvement has occurred, the management is in general not different from that of other varieties of chronic renal failure. A high proportion of patients develop blindness in association with this type of renal failure. Edema becomes increasingly difficult to relieve. Some degree of congestive cardiac failure usually occurs. In the earlier stages a moderate protein intake is allowed if the urea nitrogen is stable. Diuretics are used together with a modest restriction of sodium to one gram or less daily, provided this does not produce an increase in azotemia. Aldosterone antagonists may be

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tried as the edema becomes resistant. When the blood urea nitrogen is rising, the dietary protein is restricted to 30 grams a day or less. Pyelonephritis is treated with appropriate antibiotics.

Case Report

This 47-year-old white male was first admitted to Mt. Sinai Hospital on 2-5-63 because of dyspnea, leg edema, and a chronic left heel ulcer. Diabetes mellitus had been present for 22 years and treated with 25 units NPH insulin. The condition had not required insulin prior to 1945, at which time, following an episode of pneumonia, he took insulin for a three-month period. About eight months prior to this admission he had been put back on insulin. The symptoms resulting in this hospitalization had begun two weeks before admission.

Physical examination revealed a blood pressure of 120/80. The retinae contained small hemorrhages with whitish exudates. Bilateral pleural effusion was present, and there were moist rales at both lung bases. The heart was enlarged to percussion, and the liver was palpable three cm. below the right costal margin. There was atrophy of interossei muscles of both hands, and pretibial and ankle edema. There was a large yellowish ulcer with surrounding induration on the left heel. Neurological examination revealed hypoactive to absent deep tendon reflexes in the lower extremities. Sensation was reduced in both legs and vibration sense was impaired in the left leg.

Blood urea nitrogen was 50 mg.%, fasting blood sugar 273 mg.%, total serum protein 6 gm.%, albumin 2.8 gm., globulin 3.2 gm. Bromsulfalein test was normal. Sedimentation rate was 123 mm. in one hour and hemoglobin 9.6 gm.%. Urinalysis revealed specific gravity 1.008, 2+ albuminuria, trace of sugar, 40-50 RBC, 2-4 WBC, 30-40 hyaline casts, a few bacteria, and a few epithelial cells per hpf. An EKG showed changes compatible with myocardial ischemia.

The patient was treated for congestive heart failure, and the diabetes was controlled with 20 units of NPH insulin. Staphylococcus aureus coagulase positive was cultured from the left heel ulcer and it was treated with antibiotics. He also received vitamin B12 and Cyclospasmol.® A neurology consultant made a diagnosis of diabetic pseudotabes. Cerebrospinal fluid protein was 51 mg.%. His general condition improved, and the edema decreased. Cultures of the left heel ulceration became negative, and the ulcer was slowly healing by granulation at the time of discharge on March 2, 1963. He left the hospital on an 1800 calorie low salt diabetic diet, NPH insulin, 25 units daily, diuril 500 mgm. daily, digitoxin 0.1 mg. daily, Cyclospasmol® 200 mgm. four times daily, and vitamin B12 injections 1000 mcg. IM twice weekly. He had lost a total of 21½ pounds during his hospitalization.

He was followed in the outpatient clinic until 7-3-63 when he was admitted to the Surgical Service for skin grafting of the chronic ulcer on the left heel. Then because of increasing congestive heart failure, he was transferred to the Medical Service. He complained of sexual impotency for the first time. There were bilateral pleural effusions of a more severe degree than on the previous admission. Edema extended up to the sacrum with edema of the penis and scrotum. Femoral, popliteal, posterior tibial and dorsalis pedis pulses were all reduced. Laboratory studies at this time revealed hemoglobin 10.1 gm.%, 3+ albuminuria with 4-8 RBC and 1-3 WBC per hpf. Fasting blood sugar was 115 mg.%. Serum electrolytes were normal. Total serum protein was 5.8 gm.% with albumin 3.1 and globulin 3.7 gm.%. Blood sugars during this hospitalization fluctuated between 58 and 150 mg.%. Satisfactory diuresis was obtained with diamox and thiomerin in addition to Aldactizide, and there was a 24-pound weight loss by the time of discharge on July 16, 1963. The lower extremity edema had cleared almost completely. The ulcer on the left heel was treated with daily Dreft soaks and Panafil® ointment. He continued on Aldactizide, Digitoxin, and 20 units of NPH insulin, but Cyclospasmol was discontinued.

He was again admitted to the hospital on November 11, 1963, because of persistent ankle edema and weight gain. NPH insulin dosage had been progressively decreased because of recurrent hypoglycemia, so that his daily insulin dose on admission was only five units. There had been persistent nausea and intermittent vomiting for three months. Blood pressure was 148/90 and weight 174 pounds. There was advanced bilateral diabetic retinopathy with venous aneurysms, new vessel growth, and a large hemorrhage in the left retina. There was also marked bilateral pleural effusion and pulmonary congestion. The liver was palpable four cm. below the costal margin, and edema of the legs, the presacral area, and the penis and scrotum was marked. The ulceration of the left heel was partially healed. Hemoglobin was 9.3 gm.% There was 4+ albuminuria, specific gravity 1.015, 20-30 RBC, and 4-6 hyaline casts per hpf.

Blood urea nitrogen was 44 mg.%, and fasting blood sugar 120 mg.%. Total serum proteins were 5.4 gm.%, albumin 2.9, globulin 2.5 gm.%. Cholesterol was 167 mg.% and serum iron 41. He was treated with five units of NPH insulin daily and a strict low-salt diet. Thiomerin was used for diuresis. He was given two courses of Mannitol infusion with good diuresis after approximately 36 hours. His nausea cleared and his weight stabilized at 167 pounds.

On January 2, 1964 he was readmitted with a chief complaint of diarrhea. His blood pressure was 160/100. The fundi showed severe diabetic retinopathy with extensive hemorrhages, exudates, and microaneurysms, more marked on the right. There was massive bilateral pleural effusion. The liver was four cm. below the right costal margin and there was moderate ascites. Edema was marked, including the presacral area and the genitalia. The ulcer on the left heel was still not completely healed. Blood urea nitrogen was 79 mg.%, creatinine 3 mg.%, calcium 8.4 mg.%, phosphorous 5.8 mg.%, and fasting blood sugar 160 mg.%. Specific gravity of the urine was 1.010, albumin 2+, and glucose negative. Hemoglobin was 10.3 gm.%. He was placed on a 2,000 calorie diabetic diet and antispasmodics were used to control the diarrhea. NPH insulin was discontinued and Orinase 0.5 gm. daily started. He was also given periodic thiomerin injections. By the time of discharge the diarrhea had cleared, and the edema had subsided. A blood urea nitrogen before discharge was 40 mg.%, creatinine 2.6 mg.%, and blood glucose 110 mg.%. He was followed in the Outpatient Clinic until 3-6-64 when he was readmitted to the hospital because of intractable edema and dyspnea. During this admission he responded poorly to diuretic and cardiac management and required two thoracenteses to relieve dyspnea. Still edematous he was discharged at his request and died suddenly on 3-25-64 while at home. Permission for autopsy was not granted.

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Lose no time; be always employed in something useful; cut off all unnecessary actions.—Benjamin Franklin

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Abstracts, Briefs and Commentaries

POSTOPERATIVE WOUND INFECTIONS

A 192-page report has been submitted on a co-operative study by five academic institutions over a two-year period in an attempt to fully evaluate the influence of ultraviolet irradiation in the operating room on the incidence of postoperative wound infection.

The irradiation reduced the number of airborne bacteria in the operating room, but the wound infection rate was unchanged. Significant improvement did occur from 3.8 to 2.9 per cent infection rate in the refined-clean group. However, this was offset by an apparent detrimental effect in the nonclean wounds.

Secondary information was gathered in other aspects of the postoperative infection problem. It was found that diabetic patients showed no increased susceptibility to infection when compared to nondiabetics of similar ages. Steroid therapy appears to affect wound infection rates adversely. Extremely obese patients appear to be more susceptible to wound infection. Little evidence was found that a malnourished patient is more susceptible to infection. Patients who harbor infection remote from the operative incision are likely to have a greater wound infection rate. The duration of operation brings an increase of wound infection rate — the longer the operation, the more likely wound infection will appear. Thus duration appears to be the primary determinant of risk of infection.

The duration of preoperative hospitalization appears to influence the infection rate independently. The use of prophylactic antibiotics was associated with a much higher wound infection rate. However, the authors qualify this observation by the notation that obvious case selection may well be of significance, and state that only further carefully controlled studies can settle this issue of prophylactic antibiotics by a thoroughly randomized study.

J. H. Strickler, M.D.
Minneapolis, Minnesota

The Influence of Ultraviolet Irradiation of the Operating Room and Various Other Factors. Supp to Ann Surg 160:August, 1964.

TREATMENT OF INFECTIOUS MONONUCLEOSIS

Since 1958 reports of dramatic response of infectious mononucleosis patients to chloroquine have appeared, but controlled studies apparently have not been made. This paper reports a double-blind study of 40 patients, half of whom were given chloroquine and the other 20 a placebo. Based on results, the authors conclude that the drug is beneficial in that it appears to shorten the course of the disease. The results, however, do not appear to confirm earlier reports of consistent dramatic responses to chloroquine, nor do they suggest that it would be reliable as a diagnostic test. Here are the comparative average durations in days for the 20 patients on chloroquine and the 20 on the placebo: (a) Hospitalization: placebo, 14; treated, 8.7; (b) Pharyngitis: placebo, 7.1; treated, 4.6; (c) Subjective Symptoms: placebo, 8.3; treated, 5; (d) Hepatomegaly: placebo, 11.8; treated, 6; (e) Fever: placebo, 7.1; treated, 5.3; (f) Liver Function Abnormalities: placebo, 10.5; treated, 9.2; (g) Splenomegaly or Lymphadenopathy: placebo, 9.6; treated, 7.1.

The patients were males ranging in age from seventeen to twenty-five (average 20.5 years) admitted to an army hospital over a six-month period. All of them fulfilled criteria for a conclusive diagnosis of infectious mononucleosis: absolute lymphocytosis with atypical lymphocytes; significant lymphadenopathy, fever, pharyngitis, and a changing heterophile antibody titer reaching a peak of 1:224 or greater. Placebo and active tablets were identical in appearance, with the number on the treatment box the only key to the identity of the agent received from the pharmacy. Patients were not aware that any study was being made. Which patients were chloroquine-treated or which received the placebo was not known until after final outpatient evaluation had been completed. Chloroquine dosage was 1 gram immediately; 0.5 gram in eight hours; 0.5 gram daily for nine days; and 0.025 gram daily for eight more days. At first patients were put on bed rest. Bathroom privileges were limited. Ambulation was permitted when temperatures became normal and spleen size was regressing. They were discharged to duty three to four days after the final temperature elevation. The authors describe laboratory procedures, not reviewed here. A daily check list on each patient was kept on a work sheet. Items were: general condition, throat condition, lymphadenopathy, spleen size, liver size, skin eruption, per cent of diet eaten, and any signs of drug reaction. Temperature and pulse were recorded every eight hours.

The authors discuss findings at some length. In answer to the question of whether all infectious mononucleosis patients should be given chloroquine the authors note that the study was too small to supply a definitive answer. They add, however, the following favorable points: (a) the cost of chloroquine is low; (b) if morbidity is reduced by only 20 per cent the saving in man hours would be worth while; and (c) chloroquine appears relatively safe for short-term use. In this series no serious side effects were noted.

Medical Abstract Service
Berwyn, Ill.

Cowley, R., and Myer, J.: Ann Intern Med 57:937, 1962

LUMBAR SYMPATHECTOMY

The effect of lumbar sympathectomy upon blood flow to the skin and muscles of the lower extremities in eight patients with arteriosclerosis obliterans was measured plethysmographically. Twelve limbs were so measured. Six unilateral sympathectomies were performed and the post-sympathectomy data was available. The nonsympathectomized contralateral extremity was studied in three patients. Patients were studied by aortography and all demonstrated arteriosclerosis obliterans in the iliofemoral popliteal system not amenable to direct arterial reconstruction or graft. Patients with gangrene, loss of tissue, or ulcerations were not included. The lumbar sympathectomy consisted of removal of the sympathetic chain L1 through L4.

A constant environmental laboratory was kept standard in all experiments. Blood flow in the skin and muscle were tested under various physiologic dilator stimuli and drug vasodilator stimuli. The responses of the unoperated limb did not appear to be affected in any of the parameters measured.

It was the authors' conclusion that the early effects, 2-4 weeks postoperatively, of lumbar sympathectomy upon blood flow to the lower extremity appeared undesirable except for an increase in perfusion of the resting skin. There did not appear to be any "borrowing-lending" phenomena from one extremity to the other. Blood flow responses in the unoperated extremity were not altered by the sympathectomy on the contralateral side.

Jerome T. Grismer, M.D.
Minneapolis, Minn.

Tice, D. A., Reed, G. E., Messina, E. J., Clemente, E., and Redisch, W.: Effects on Vascular Response in the Lower Extremities of Patients with Arteriosclerosis Obliterans. AMA Arch Surg 87:461, 1963

GUILLAIN-BARRE SYNDROME

The world literature on corticotropin and glucocorticoid therapy of the Guillain-Barre syndrome is reviewed pointing out that differences and discrepancies in diagnostic criteria, methods of therapy, and modes of reporting make the results difficult to evaluate. Eighteen patients treated with these hormones at the University of Michigan Medical Center are presented and compared with 17 nontreated patients who, however, did not constitute a true control group. The patients in both groups survived, but there was a suggestively favorable response in most of those receiving hormone therapy. Some of the difficulties in evaluating the results of this treatment are discussed. Further hormonal therapy in this condition seems justified, not only to give patients the benefit of the therapeutic response thus far demonstrated, but also to clarify the effect of such treatment and its relationship to the etiology and pathogenesis of the syndrome.

Courtesy of References and Reviews
Journal of the American Medical Association

Heller, G., and DeJong, R.: Arch Neurol 8:179, 1963

PERITONEAL DIALYSIS IN SALICYLATE POISONING

Four cases of salicylate intoxication were treated by continuous peritoneal dialysis. Observations showing the extensive depletion of available body base, especially potassium are reported. The clinical states appear to parallel these, rather than the serum salicylate levels. During dialysis the major repair process is correction of electrolyte depletions, which permits the effective renal excretion of salicylate. The various therapeutic measures available for treating salicylate intoxication are reviewed. Peritoneal dialysis is the simplest and most freely available of these. It is suggested on the basis of this experience that prevention

Continued

of salicylate intoxication now depends largely on accuracy of information in manufacturers' advertising.

Courtesy of References and Reviews
Journal of the American Medical Association

Elliot, G., Crichton, J., and Miller, G.: Anesth Analg 42:338, 1963

LEAD EXPOSURE IN PAINTERS

Single blood lead concentration determinations were done among 107 male decorative and house painters employed by the Federal General Services Administration in the Washington, D.C. area. No elevated blood lead levels were found, the mean for the group being 0.023 mg. of lead per 100 gm. of whole blood, and the range from 0.013 to 0.040. This mean level approximated that of a control group of five males and the recently reported mean blood concentration value of an urban male population. The federal painters' practices are thought to be representative, and their risk of lead poisoning associated with current materials and methods of application used in the decorative and house painting trades appears to be negligible. Within the painter group, no significant relationship between blood lead values were associated with age, methods of application, or number of years engaged in the painting trades.

Courtesy of References and Reviews
Journal of the American Medical Association

Siegel, G.: Arch Environ Health 6:720, 1963

ANAL FISTULAS

There are two groups of anal fisulas: 5 percent are complex and difficult to deal with, while 95 percent are simple and easily cured.

There is no difficulty in distinguishing a simple from a complex fistula. The track of a simple fistula can be palpated as a thick, fibrous cord running from the external opening towards the anal canal. A probe passed through the track lies transversely to the axis of the rectum.

In the complex fistula no track can be palpated subcutaneously and the probe passes upward parallel to the axis of the rectum for six to seven cm. to the apex of the ischiorectal fossa. On rectal examination a horseshoe induration is felt just below the level of the anal ring.

The orthodox treatment is to lay open the whole track, so as to convert it into a racket-shaped wound. If this were done in a simple fistula, on a desert island, with no other treatment except a morning and evening swim in the sea, the fistula would heal. The complex fistula is a different matter.

To lay open a horseshoe fistula requires an incision in the perianal skin involving almost the entire circumference of the anus. To flatten the wound adequately requires the sacrifice of a large amount of skin and the resulting wound may take eight to ten weeks to heal.

The fistula whose internal opening lies above the anorectal ring cannot be treated by the classical method without producing incontinence. Fear of dividing too much of the sphincter muscle and rendering the patient incontinent is often responsible for the inadequate treatment.

With a knowledge of the etiology and the relation to the sphincter muscles, healing of a simple fistula by orthodox methods presents no problems. Complex fistulas may tax the patient's endurance and the surgeon's skill to the utmost.

Courtesy of World-Wide Abstracts

Thompson, H.: Proc Roy Soc Med 55:9:754

KVEIM TEST FOR SARCOIDOSIS

A "double-blind" study of the Kveim test was undertaken in a test-series of patients with active and inactive sarcoidosis on and off steroid therapy, and in a contratest series that included patients with active tuberculosis and normal subjects with negative tuberculin reactions. This study led to the following conclusions: (1) When properly performed with antigen prepared from sarcoid tissue, the Kveim test is a specific diagnostic tool for detection of patients with active sarcoid. (2) Patients with inactive sarcoid may give positive or negative reactions, but patients who do not have sarcoid do not have a positive Kveim reaction when injected with a good sarcoid antigen. (3) Steroid therapy in active sarcoidosis does not prevent a positive Kveim reaction. (4) Antigen prepared from normal tissue may give reactions resembling "foreign body giant cell granuloma" only in patients with active sarcoid, suggesting a special hypersensitivity to foreign tissue rather than antigen-antibody relationship. (5) There is no necessity to perform a biopsy in a patient who has not developed a macroscopic lesion, but histopathological examination of gross lesions is always necessary.

Courtesy of References and Reviews
Journal of the American Medical Association

Kenney, M. and Stone, D.: Amer Rev Resp Dis 87:503, 1963

OTITIS EXTERNA

Virtually all manifestations of otitis externa are controllable by the administration of an acid alcohol, or acid alcohol-hydrocortisone, solution. This result, however, is accomplished only after thorough cleaning of the external canal. Cleaning is done painlessly with a proteolytic enzyme ointment as a debriding agent. Therapy is begun only after the external canal is clean. Complete remission of symptoms was obtained in an average of 4.4 days, without any evidence of sensitization to the preparations used.

Courtesy of References and Reviews
Journal of the American Medical Association

Jenkins, B.: Arch Otolaryng 77:442, 1963

DIRECT VISION ADENOIDECTOMY

One item in any program to prevent hearing loss is safeguarding the eustachian tube during adenotonsillectomy. Since this procedure is the most frequently performed operation in the United States, precautions assume particular importance. The best way of doing this, says the author, is to rely on direct preoperative inspection, direct observation during surgery, meticulous surgical technic, and postoperative inspection and follow-up. Removal of adenoid tissue under direct vision or with the help of a large pharyngeal mirror is better than relying on blind procedures done by sense of touch, which may result in leaving adenoid tissue remnants or danger to the eustachian tube. Damage to this orifice during adenoid surgery is not too uncommon, causing persistent serous otitis media which may lead to adhesive otitis media. Of 500 consecutive cases having adenoid and/or tonsil operations, 53 (10.6 percent) were revision adenoidectomies. Only one of these latter had been originally operated on by direct vision. Every one of the revisions (100 per cent) had transient or permanent hearing loss as the chief complaint. Chronic otitis media was present in 21.1 percent; onset was after the first operation. While frank stenosis and evidence of eustachian tube injury was present in 9.6

Continued

percent, none of these had chronic middle ear infection, but all showed signs of persistent or recurrent serous otitis media.

Even in children too young to be co-operative, preoperative evaluation is possible after shrinkage of the nasal membranes by anterior rhinoscopy. Most opportune is the time before surgery when the child is fully anesthetized. The lower two-thirds of the nasopharynx can be exposed by means of using the various models of palate restractors, the hooked end of a Davis tongue blade, or 2 rubber catheters introduced through the nostrils and grasped in the pharynx. The upper third can be inspected with a large pharyngeal mirror dipped in any soapy solution to prevent fogging. For the vault, palpation with the finger is unsatisfactory except for the lateral nasopharyngeal wall with the tube orifices.

A preferred method is use of both a square and a narrow, long curette, the latter serving as a palate elevator which, with the laryngeal mirror in place, can be positioned properly to remove with one stroke the total amount of central adenoid tissue. Firm contact is obtained with the superior edge of the posterior septum. With the left thumb as a fulcrum, the curette is guided inferiorly, keeping contact until the superior border of the superior constrictor muscle is approached, when the contact pressure is released. Use of a sharp cutting edge minimizes danger of tearing the superior constrictor muscle. Now a long narrow curette is introduced into the superior recess of the right fossa of Rosenmuller. Here care is taken not to engage the tubal orifice; this is done by tilting the curette handle to the right. This is repeated on the left side. Postoperatively, the nasopharynx is inspected again. Bleeding having stopped by this time, remnants of lymph tissue will be revealed by aspiration of blood clots. This also will prevent aspiration of clots from the nose later. Bits of lymph tissue may be easily removed by triangular biopsy forceps.

Courtesy of Medical Abstract Service
Berwyn, Illinois

Kossner, Herbert K.: Eye Ear Nose Throat 42:52, 1963

RUNAWAY CHILDREN

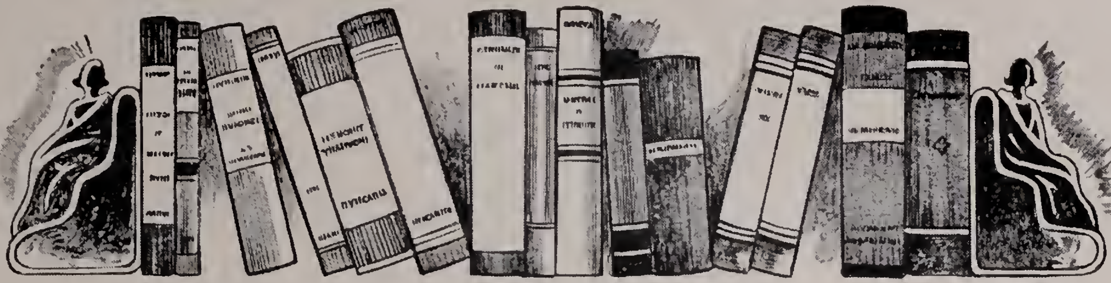
Self-estimates of children in regard to their degree of control over external events (dimension of outer control to uncontrol) were measured on the basis of ratings of clinical interview data. Forty-two runaways, of both sexes, with a median age of 13.5 years, were compared with a similar group of non-runaway disturbed children. The runaways were rated as experiencing significantly more outer uncontrol on three relevant scales. The interpretation is that, on a gradient of generalized control-uncontrol, the more experience there is of losing control, the more likely it is that extreme behavior, such as running away from home, will eventuate.

Courtesy of References and Reviews
Journal of the American Medical Association

Leventhal, T.: Arch Gen Psychiat 9:122, 1963

The great question which, in all ages, has disturbed mankind, and brought on them the greatest part of those mischiefs which have ruined cities, depopulated countries, and disordered the peace of the world, has been, not whether there be power in the world, not whence it came, but who should have it.—John Locke

Inflation is repudiation.—Calvin Coolidge



Book Reviews

I love to lose myself in other men's minds. When I am not walking, I am reading. I cannot sit and think; books think for me.—Charles Lamb

MODERN TREATMENT — **Vol. 1, Nos. 2, 3, and 4, March, May, and July, 1964. By various authors. Harper and Row, New York. A Bimonthly publication, $16.00/year.**

The plan of this new series of books apparently is to assign a subject to a guest editor and to publish bimonthly under the general heading "Modern Treatment." The three books considered here take up lung and liver disease in the February issue; anemias and cardiac arrhythmias in May; and infectious diseases in July. "Treatment" is a magic word in medical publications attracting readers who might not respond to such a title word as "diagnosis." The problem is nicely put by Edwin Bayrd: "Consider the 55 year old tired housewife, whose anemia responds gratifyingly to iron, who finds a year later that her silent cecal carcinoma has now metastasized. Less tragic is the 60 year old farm wife who has received weekly injections of liver and 16,425 pills over a period of 15 years without any improvement in her anemia or myxedema." The greatest drawback of this series is that several of the authors have taken their therapeutic assignments literally, neglecting discussion of other aspects upon which treatment is based. The day has not passed, Bayrd to the contrary, that diagnosis before therapy needs be stressed. With this reservation the reviewer learned much about therapy from these volumes. Forthcoming subjects in this series will include headache, menstrual disorders, arthritis, epilepsy, acid peptic disease. All of these subjects should be interesting to the medical profession. The editing leaves something to be desired. Forgiveable is the parenthetic (32.9° F.) to explain the 0.5° C. which is the greatest allowable difference between mouth and rectal temperatures. Sixteen blank pages which crop up two at a time in the copy of "Infectious Diseases" are downright irritating.

Reuben Berman, M.D.
Minneapolis, Minnesota

BETTER HEALTH FOR WOMEN — **Charles Richard Alsop Gilbert, M.D., Doubleday & Co., 1964, $4.95 365 pages**

This book is written principally for the woman patient. It deals fully with functional, organic, and physiologic phases from the beginning of puberty to the adult life.

Each chapter contains a series of questions and answers. The nine or ten illustrations in the book seem to be adequate, as in a book of this nature there is no need of extensive anatomical drawings or technical procedures.

This book would be superfluous for the physician and is essentially for the woman patient. Doctors could well afford to give this book to their apprehensive gynecologic patients.

Carl O. Rice, M.D.
Minneapolis, Minnesota

EARLY TREATMENT OF FACIAL INJURIES — **Thomas John Zaydon, James Barrett Brown, Leo & Febiger 1964, No price listed**

This is a short, concise, but detailed monograph on facial injuries, excluding the eye, that should appeal to any physician who cares for patients with acute trauma. Although certain of the techniques of reduction of the facial bones after fracture will not be applicable to other than a specialist in that field, the knowledge to be gained by reading those chapters should be of great help to all physicians treating the less extensive facial injury.

The chapter on soft tissue wound care is a model of clarity, yet obviously represents the authors' tremendous experience in plastic surgery. This in an excellent book and should prove to be quite popular.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

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Perinatal Mortality Study

Characteristic Facies Associated with Bilateral Renal Agenesis

Case Report

The 20-year-old mother of this infant was Rh positive and this was her first pregnancy. She had no illness or drugs during the pregnancy, and at 7½ months spontaneously went into labor and had a double footling delivery of a male infant weighing 3 pounds, 12 ounces. No anesthetics were used during the delivery.

The infant was cyanotic and gasping. The ears were low-set, "floppy," folded and malformed. There was a wide epicanthal fold bilaterally which extended out over the malar bones. Periorbital edema was present. The jaw appeared to recede, giving the face a "pinched" appearance. Rales were heard throughout all lung fields. The liver was palpable 2 cm. below the right costal margin. There was an equinovarus deformity of the left foot. In spite of positive pressure oxygen therapy, the respirations diminished and the child died 2 hours, 45 minutes following birth.

Autopsy on the infant revealed both kidneys and ureters to be absent. The urachus was present and ended in a string-like urinary bladder. The urethra was patent. The testes were intra-abdominal. The adrenals together weighed 6.8 grams and were flat, hyperemic, closely apposed to the psoas muscle bilaterally. The lungs were normal in configuration but small in size. They were not weighed apart from the heart which was normal. The heart and lungs together weighed 35.5 grams. Microscopic sections of the lungs showed severe atelectasis. The remainder of the organs were normal for a premature infant.

Comment

Potter[1] describes characteristic facies associated with bilateral renal agenesis, enabling the condition to be diagnosed at birth. She states, "The facial expression is generally that of extreme age and is characteristic enough to warrant a diagnosis of renal agenesis from inspection of the face alone. This appearance seems to be related to lack of kidney function rather than to the specific malformation because a somewhat similar appearance is found in some infants with fatal polycystic changes or extreme renal hypoplasia.

"The most constant facial characteristic is a very prominent epicanthic fold that forms a semicircle arising on the forehead, swinging down to cover the medial palpebral commissure and ending on the cheek. It is different from the fold in mongolism, which ordinarily ends at the level of the commissure. The nose is usually flattened, the depression below the lower lip is unusually prominent and the ears ordinarily contain little cartilage, are flat without a formed helix and often are set at an angle exceptionally low on the sides of the head.

"Intrauterine life does not appear to be hampered by absence of kidneys, for many of these infants are born normally at term. Because waste products are successfully eliminated via the placenta, urinary secretion is not necessary to maintain intrauterine life. The longest survival in our series was 11 hours. Death of all the live-born infants was preceded by dyspnea, cyanosis and evidence of respiratory embarrassment. The lungs of all were hypoplastic, and this pulmonary abnormality was fatal before the absence of the kidneys could cause death from uremia."

Schaffer[2] verifies Potter's description of the facies associated with bilateral renal agenesis and states that almost all the subjects are male.

Continued

Ramsey County Perinatal Mortality Study Committee.

Summary

A case of bilateral renal agenesis associated with characteristic facies as described by Potter[1] is presented. The presence of bilateral wide epicanthic folds extending out over the malar bones with low-set, "floppy," malformed ears should alert the physician to the correct diagnosis and ultimate prognosis in these infants.

The Ramsey County Perinatal Study Committee strongly encourages autopsies in all perinatal deaths. In this way, important information may be gained from these fetal and neonatal deaths.

References

1. Potter, Edith L.: Pathology of the Fetus and Infant, Yearbook, Medical Publishers, Inc., Chicago, Second Edition 1961, page 430.
2. Schaffer, Alexander J.: Diseases of the Newborn, W. B. Saunders Co., Philadelphia, 1960, page 421.

Three M's in the Renaissance

Medicine's progress in the Renaissance was distinguished for its resolute and heroic effort to repudiate its heritage of superstition and magic by identifying itself with the current scientific advances of the period. Chemistry and biology were still in their infancy; only mathematics and mechanics had attained a reputably mature status. So medicine, eager to turn its back on past errors and follies, attempted to synthesize its principles with those of mathematics and mechanics.

"The experimenters began to weigh and measure the various parts of man, as if he were so much brick, cement and lead piping. So it was reckoned that the muscles moving the thumb weighed 122 grains and they were estimated to develop a power of 3,270 pounds; accordingly the stomach, although weighing only eight ounces, could generate a force of 117,088 pounds, increasing to 461,219 pounds when the muscles of the abdomen and diaphragm were working full strength. Fruitless efforts were made to calculate the weight of an individual spermatozoon. The most logical absurdity, however, that arose from the school of 'physical' medicine, was the mathematical theory which worked out the span of life depending on the number of times a man's heart had been geared to beat. So that if a person had a heart fixed to last seventy years provided it beat at an average rate of sixty times a minute, then too much excitement which raised the heart beats to an average of seventy-five a minute would automatically determine the man's end at fifty-six years."*

However implausible the results of medicine's synthesis with mathematics and mechanics, they were historically significant in marking medicine's emergence into the light of rational thinking and scientific practice.

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*Leff, S., M.D., D.P.H.: From Witchcraft to World Health. The MacMillan Co., New York, p. 119, 1958.

Don't part with your illusions. When they are gone you may still exist, but you have ceased to live.—Mark Twain

Special Article

Rheumatic Fever

Minnesota Secondary Prevention Program Part II—Recurrences[*]

LAWRENCE V. PERLMAN, M.D.[**]
DEAN S. FLEMING, M.D.[***]
THOMAS J. THOM[†]
Minneapolis, Minnesota

THE PURPOSE of the Minnesota Rheumatic Fever Secondary Prevention Program is the prevention of recurrent rheumatic fever by professional education, the maintenance of a medical registry, and the provision of low cost prophylaxis. This program was designed as a service project and not as a research program, because the effectiveness of prophylactic sulfadiazine and penicillin has been demonstrated in many studies.[1,2] However, in order to assess the effectiveness of this particular program, the Minnesota Department of Health, in consultation with the Rheumatic Fever Committee of the Minnesota Heart Association and the Heart Committee of the Minnesota State Medical Association, has been collecting data on reported recurrences of rheumatic fever and streptococcal infections.

The purpose of this report is to record and comment upon these recurrences for the first four years of operation of the program — January 27, 1960 to January 27, 1964 — among the first 8,604 patients registered.

Mode of Operation

A recurrence of rheumatic fever or a streptococcal infection may be reported in one of two ways. First, attached to each book of prescriptions mailed to the physician for patient use is a post card by which the physician may notify the Heart Disease Control Program of the Minnesota Department of Health of an episode of acute rheumatic fever (Figure 1). Second, every twelve months the physician is sent a reapplication form on which he indicates whether or not the patient has had a recurrence of rheumatic fever or a streptococcal infection (Figure 2). The majority of recurrences are noted in the latter manner. If there is indication by one of these means that a recurrence or a streptococcal breakthrough has occurred, a second form (Figure 3) is sent to the physician asking him to describe the episode in detail.

Continued

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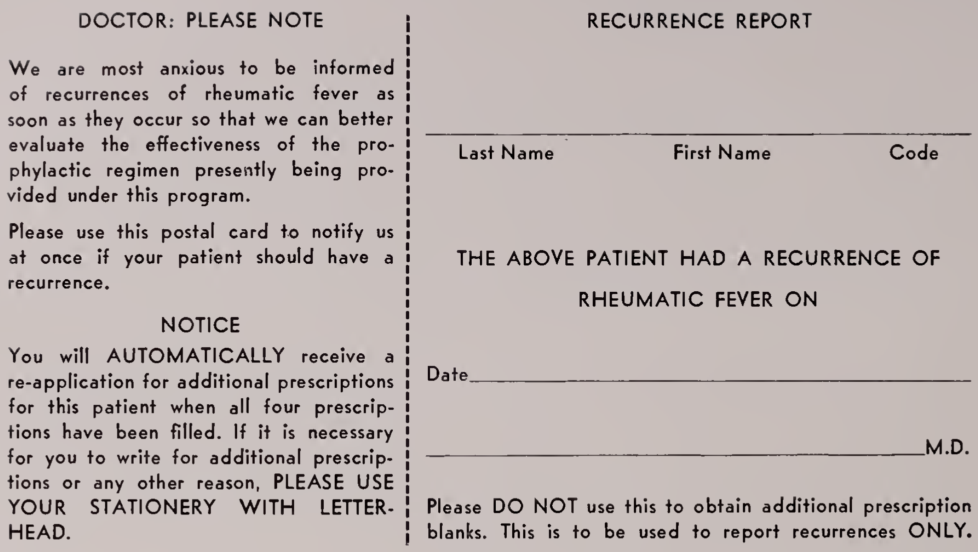
[*] Part I-Minnesota Med. 47:12, page 1551.

[**] Heart Disease Control Officer, Heart Disease Control Program, Public Health Service, U. S. Department of Health, Education and Welfare, assigned to Minnesota Department of Health, Minneapolis, Minn.

[***] Director, Division of Disease Prevention and Control, Minnesota Department of Health, Minneapolis, Minn.

[†] Student, School of Public Health, University of Minnesota, Minneapolis, Minn.



DOCTOR: PLEASE NOTE

We are most anxious to be informed of recurrences of rheumatic fever as soon as they occur so that we can better evaluate the effectiveness of the prophylactic regimen presently being provided under this program.

Please use this postal card to notify us at once if your patient should have a recurrence.

NOTICE

You will AUTOMATICALLY receive a re-application for additional prescriptions for this patient when all four prescriptions have been filled. If it is necessary for you to write for additional prescriptions or any other reason, PLEASE USE YOUR STATIONERY WITH LETTERHEAD.

RECURRENCE REPORT

Last Name First Name Code

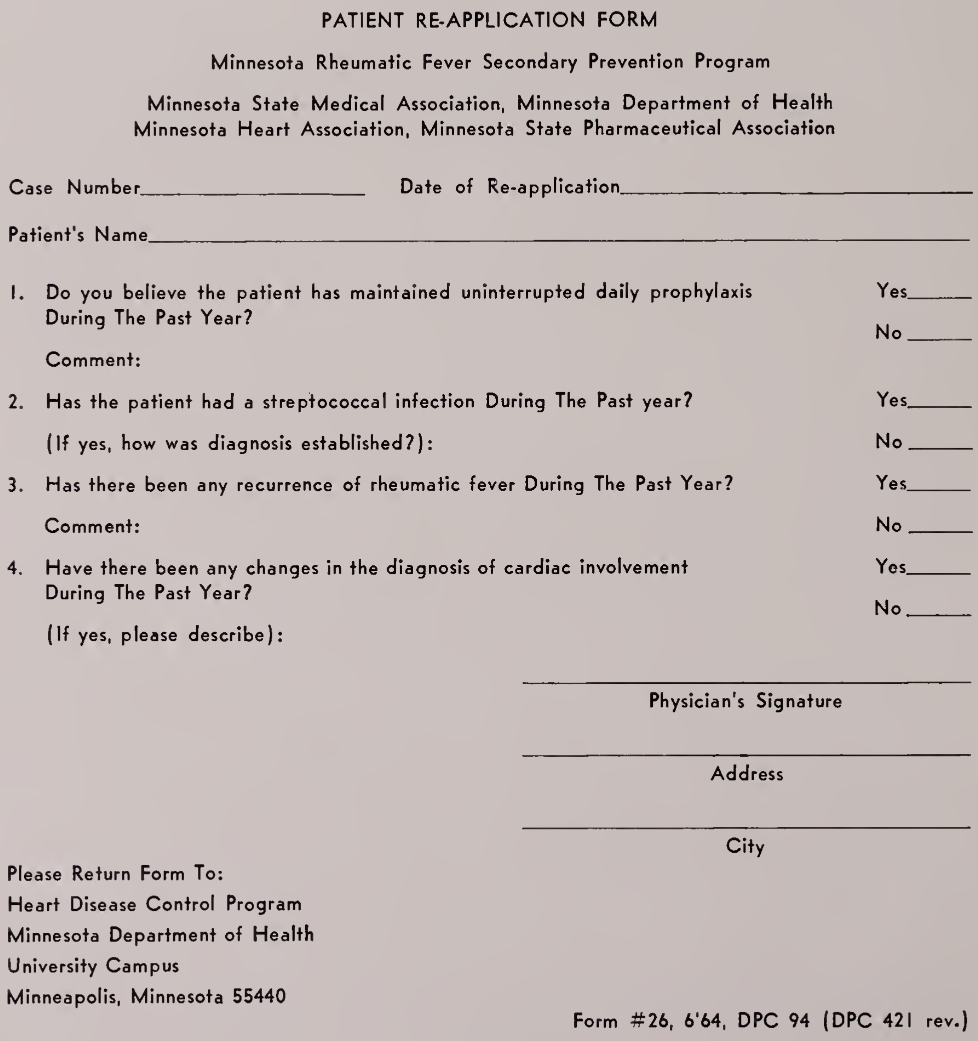
THE ABOVE PATIENT HAD A RECURRENCE OF RHEUMATIC FEVER ON

Date____________________

____________________M.D.

Please DO NOT use this to obtain additional prescription blanks. This is to be used to report recurrences ONLY.

Figure 1



PATIENT RE-APPLICATION FORM

Minnesota Rheumatic Fever Secondary Prevention Program

Minnesota State Medical Association, Minnesota Department of Health
Minnesota Heart Association, Minnesota State Pharmaceutical Association

Case Number____________ Date of Re-application____________

Patient's Name____________________

1. Do you believe the patient has maintained uninterrupted daily prophylaxis During The Past Year? Yes____ No ____
   Comment:
2. Has the patient had a streptococcal infection During The Past year? Yes____ No ____
   (If yes, how was diagnosis established?):
3. Has there been any recurrence of rheumatic fever During The Past Year? Yes____ No ____
   Comment:
4. Have there been any changes in the diagnosis of cardiac involvement During The Past Year? Yes____ No ____
   (If yes, please describe):

____
Physician's Signature

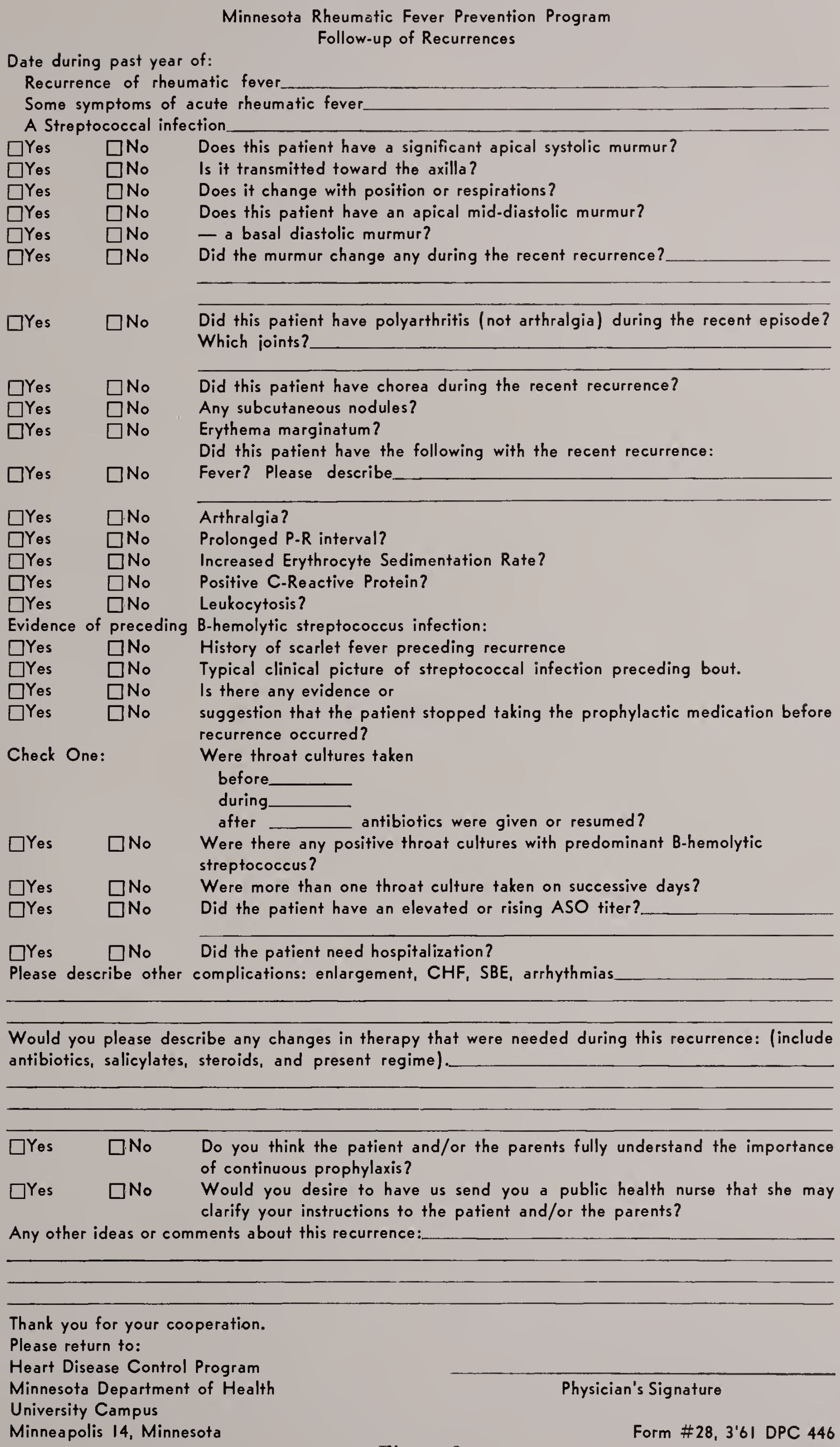
____
Address

____
City

Please Return Form To:
Heart Disease Control Program
Minnesota Department of Health
University Campus
Minneapolis, Minnesota 55440

Form #26, 6'64, DPC 94 (DPC 421 rev.)

Figure 2



Minnesota Rheumatic Fever Prevention Program
Follow-up of Recurrences

Date during past year of:
Recurrence of rheumatic fever__________
Some symptoms of acute rheumatic fever__________
A Streptococcal infection__________

☐Yes ☐No Does this patient have a significant apical systolic murmur?
☐Yes ☐No Is it transmitted toward the axilla?
☐Yes ☐No Does it change with position or respirations?
☐Yes ☐No Does this patient have an apical mid-diastolic murmur?
☐Yes ☐No — a basal diastolic murmur?
☐Yes ☐No Did the murmur change any during the recent recurrence?__________

☐Yes ☐No Did this patient have polyarthritis (not arthralgia) during the recent episode? Which joints?__________

☐Yes ☐No Did this patient have chorea during the recent recurrence?
☐Yes ☐No Any subcutaneous nodules?
☐Yes ☐No Erythema marginatum?
Did this patient have the following with the recent recurrence:
☐Yes ☐No Fever? Please describe__________

☐Yes ☐No Arthralgia?
☐Yes ☐No Prolonged P-R interval?
☐Yes ☐No Increased Erythrocyte Sedimentation Rate?
☐Yes ☐No Positive C-Reactive Protein?
☐Yes ☐No Leukocytosis?
Evidence of preceding B-hemolytic streptococcus infection:
☐Yes ☐No History of scarlet fever preceding recurrence
☐Yes ☐No Typical clinical picture of streptococcal infection preceding bout.
☐Yes ☐No Is there any evidence or
☐Yes ☐No suggestion that the patient stopped taking the prophylactic medication before recurrence occurred?
Check One: Were throat cultures taken
before__________
during__________
after __________ antibiotics were given or resumed?
☐Yes ☐No Were there any positive throat cultures with predominant B-hemolytic streptococcus?
☐Yes ☐No Were more than one throat culture taken on successive days?
☐Yes ☐No Did the patient have an elevated or rising ASO titer?__________

☐Yes ☐No Did the patient need hospitalization?
Please describe other complications: enlargement, CHF, SBE, arrhythmias__________

Would you please describe any changes in therapy that were needed during this recurrence: (include antibiotics, salicylates, steroids, and present regime).__________

☐Yes ☐No Do you think the patient and/or the parents fully understand the importance of continuous prophylaxis?
☐Yes ☐No Would you desire to have us send you a public health nurse that she may clarify your instructions to the patient and/or the parents?
Any other ideas or comments about this recurrence:__________

Thank you for your cooperation.
Please return to:
Heart Disease Control Program
Minnesota Department of Health
University Campus
Minneapolis 14, Minnesota

____
Physician's Signature

Form #28, 3'61 DPC 446

Figure 3

THE ST. PAUL
INSURANCE COMPANIES

. . . OK, SHOOT!

Immunize yourself from the constant worry of liability suits with The St. Paul's Professional Liability Coverage. It protects you in allegations of professional negligence arising from patient care, plus civil suits alleging assault and battery, libel and other charges. Easily combined, if desired, with your other insurance coverages including life, homeowners, group health, etc. in a single St. Paul Multicover Plan. Gives you the most complete, most convenient coverages available today with just one agent, one premium, one convenient package.

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St. Paul Mercury Insurance Company
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PSYCHIATRY FOR THE MEDICAL PRACTITIONER

New Orleans, Louisiana March 4-6, 1965

Sponsored by the DIVISION OF NEUROLOGY AND PSYCHIATRY OF TOURO INFIRMARY
under a National Institute of Mental Health Grant

GUEST LECTURERS INCLUDE:

Jack Ewalt, M.D., Prof. of Psychiatry, Harvard Med. School, Past Pres. of American Psychiatric Association, Boston, Mass.

John Lambert, M.D., Medical Director, Four Winds Hospital, Katonah, N. Y.

Zigmond Lebensohn, M.D., Chief, Dept. of Psychiatry, Sibley Memorial Hospital, Washington, D. C.

William Sheeley, M.D., Director of Psychiatry & Medical Practice Project of the A.P.A., Washington, D. C.

Philip Solomon, M.D., Chairman, A.P.A. Committee on Medical Practice, Boston, Mass.

Course will be given at Jung Hotel, 1500 Canal Street, New Orleans, La. Hotel reservations to be made directly with the Jung or hotel of your choice. Registrants who would like to enjoy Mardi Gras (March 2) are urged to make hotel reservations *immediately.*

Guest speaker for the luncheon on March 4 will be GEORGE BURCH, M.D., Henderson Professor and Chairman, Dept. of Medicine, Tulane Medical School. Subject: *"Emotions and Cardiovascular Disease."* Cost of luncheon included in registration fee. At the end of Friday's session, there will be a dutch treat two-hour cocktail party with George Lewis and his band from Preservation Hall entertaining.

AMONG TOPICS TO BE DISCUSSED:

"Detection of Incipient Psychiatric Disorders During a General Medical Examination"
"Medical Practitioners and Supportive Handling of Schizophrenia"
"Adolescents — Disturbed and Disturbing"
"The Physician and His Reaction to the 'Crock' "
"Newer Thoughts About the Therapy of Alcoholism"
"Medical Conditions with Psychiatric Manifestations"
"Recognition and Treatment of Depressive Reactions by Medical Practitioners"
"Treatment of Emotional States by the Medical Practitioner"

Gene L. Usdin, M.D., Chief
Division of Neurology & Psychiatry
Touro Infirmary
3516 Prytania Street
New Orleans, La. 70115

Enclosed is my registration fee of $20 for the *"Psychiatry for the Medical Practitioner"* course to be given March 4-6, 1965, at the Jung Hotel. (Checks should be made payable to Touro Infirmary.)

Name ______________________________

Address ____________________________

____

Results

In the first four years of the program, 235 recurrences of rheumatic fever and 262 episodes of acute streptococcal infections were reported. Detailed information was obtained through a follow-up questionnaire (Figure 3) on 81.7 per cent (192) of the recurrent episodes and 86.6 per cent (227) of the streptococcal infections.

Table 1 summarizes the results of the 192 recurrences on which detailed information was returned. Considering only these 192, 63.2 per cent (120) met Jones Criteria. In 2.6 per cent (5) of the cases, chorea was the only major manifestation cited. The 72 cases where Jones Criteria is questionable include 28 cases where sufficient minor criteria were present but the physician was uncertain about the presence of the major criteria. In these cases the usual source of confusion was the distinction between subjective complaints of arthralgia and objective manifestations of polyarthritis. In another 44 cases minor criteria were present, but no major criteria were even suspected. These were most often patients with a past history of rheumatic fever who had vague symptomatology and low grade fever (99°-100°). More often than not these patients had no rheumatic heart disease.

The gross recurrence rate for the first four years of operation of the secondary prevention program was 1.44 recurrences per hundred years. Assuming that 63.2 per cent of all recurrences reported met Jones Criteria and allowing for a 20 per cent rate of case closure, the adjusted recurrence rate is .93 recurrences per hundred patient years.* This is comparable to the rates in both the Chicago (1.0 per 100 patient years) and the Iowa (1.3 per 100 patient years) prophylaxis programs.[3,4]

Two hundred sixty-two streptococcal infections (defined in various ways by different clinicians, but usually based on the presence of pharyngitis) were reported for an incidence of 1.61 infections per 100 patient years. Of these, 43 per cent (115) were followed by acute rheumatic fever (Table 2). Considering these 115 cases of clinical streptococcal infection followed by rheumatic disease, 17.4 per cent (20) had cultures taken (14 were positive and 6 negative). However, 30.7 per cent (45) of those 147 without rheumatic sequelae were cultured and of these 39 were positive and 6 negative.

Discussion

The fulfillment of Jones Criteria is probably the minimum requirement for a diagnosis of rheumatic fever.[5] However, there are any number of diseases which may fulfill Jones Criteria (Table 3) and still not be acute rheumatic disease. The clinical and public health significance of rheumatic fever is that it is causally related to streptococcal infection and followed in a variable number of instances by heart disease.

The occurrence of vague complaints referrable to the musculo-skeletal system and often accompanied by elevated sedimentation rates, slight leucocytosis, and low grade fever in individuals with a past history of rheumatic fever is provocative but of questionable significance. Many qualified observers feel that these illnesses are not followed by cardiac damage and if causally related to streptococcal infections should be called poststreptococcal arthralgia and not rheumatic fever.[6,7] From 20 to 40 per cent of the recurrences reported to this program fall into this category.

Expected recurrence rates among rheumatic individuals without the benefit of prophylaxis vary with age, length of time of freedom from rheumatic activity, and socioeconomic conditions. Rates vary between six and forty per 100 patient years.[8,9] The observed recurrence rate in this program is much less than these figures and it agrees with that observed in other prophylactic programs.

Two hundred sixty-two streptococcal infections were reported as of January, 1964, and of these 43.9 per cent (115) were fol-

Continued

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*The true recurrence rate lies between .93 per 100 patient years and 1.44 per 100 patient years. A certain number of individuals enrolled probably do not have rheumatic fever and therefore one has to assume that there is a constant, but not necessarily equal, observer error in diagnosing both initial and recurrent cases of rheumatic fever.

lowed by rheumatic fever. This probably represents an under-reporting of streptococcal infections which can be explained by the fact that less than half of streptococcal infections present the classic combination of fever and exudative tonsillitis. Streptococcal infections may be totally asymptomatic or manifest themselves as upper respiratory infections, nonexudative tonsillitis or brief fevers of unknown origin.[10] This underscores the necessity for continual rather than interrupted prophylaxis.

It is significant ($p > .02$) that almost twice as many throat cultures were taken in individuals with clinical streptococcal infections without subsequent rheumatic fever as opposed to those whose illnesses were followed by recurrent rheumatic disease. The purpose of doing throat cultures in individuals with increased rheumatic susceptibility is aimed at identifying the streptococcus. Eradication of streptococcal infection requires ten days of bactericidal therapy.[11] Since this is difficult and somewhat costly, the knowledge that one is dealing with the beta hemolytic streptococci is important in sustaining the physician's conviction for complete treatment.

Summary

In order to assess the effectiveness of the Minnesota Rheumatic Fever Secondary Prevention Program, the Minnesota Department of Health has been collecting data on reported recurrences of rheumatic fever and streptococcal infections in the 8,604 patients enrolled in the program from January 27, 1960 to January 27, 1964. Two hundred thirty-five recurrences were reported and detailed information was returned in 81.7 per cent (192). Of these 192, 63.2 per cent met Jones Criteria. The total recurrence rate per 100 patient years is 1.44 and the adjusted recurrence rate .93. Those rates compare with those reported in other programs.

Two hundred sixty-two streptococcal infections were reported. Of these 43 per cent (115) were followed by acute rheumatic fever. Comparing the groups that were with and without rheumatic sequelae it is noted that 17.4 per cent (20) and 30.7 per cent (45) had throat cultures taken. The importance of taking throat cultures to identify the beta hemolytic streptococci is emphasized because it sustains the necessity for ten full days of treatment of streptococcal disease.

Acknowledgements

We are indebted to Dr. Lewis W. Wannamaker, Professor of Pediatrics, University of Minnesota who reviewed the manuscript, and to Miss Katherine Gram who supervises the operation of the registry.

TABLE 1

	Number	Per cent	Per cent
Total Rheumatic Fever Recurrences	235	100.0	
Follow-up Data Submitted	192	81.7	100.0
Jones Criteria Met	120		62.5
Jones Criteria Questionable	72		37.5
Minor Criteria Present But Majors Uncertain	28		14.6
Only Minor Criteria Present	44		22.9

TABLE 2

	Streptococcal Infections			
Throat Culture	Followed by Rheumatic Fever		Not Followed by Rheumatic Fever	
Positive	14	12.2%	39	26.5%
Negative	6	5.2%	6	4.1%
None Taken	95	82.6%	67	45.6%
No Follow-up	0	0.0%	35	23.8%
Total	115	100.0%	147	100.0%

TABLE 3
Illnesses Which Mimic Acute Rheumatic Fever

- Rheumatoid arthritis
- Gonococcal arthritis
- Osteoarthritis
- Psoriatic arthritis
- Postviral arthritis
- Lupus erythematosus disseminatus
- Subacute bacterial endocarditis
- Nonspecific pericarditis with effusion
- Serum sickness (incl. manifestations of penicillin sensitivity)
- Undulant fever
- Septicemias
- Meningococcemia
- Gout
- Tuberculosis
- Poliomyelitis
- Leukemia
- Sickle cell anemia
- Sarcoidosis

Continued

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10. Feinstein, A. R.: Prophylaxis of Rheumatic Fever. Amer Heart J 67:278, 1964.
11. Denny, F., Jr.: Prophylaxis of Streptococcal Infection, *In* New York Academy of Medicine. Streptococcal Infections edited by Maclyn McCarty, New York, Columbia University Press, 1954.

Notice of Public Hearing
Minnesota State Board of Medical Examiners

"Notice is hereby given, pursuant to the provisions of Minnesota Statutes, 1961, S 15.0412, that the Minnesota State Board of Medical Examiners will hold a public hearing on Saturday, February 13, 1965, at 10 o'clock, A.M., in the auditorium of the State Office Building, Saint Paul, Minnesota, on the adoption of proposed substantive rules and regulations pertaining to professional corporations and to the practice of medicine and surgery, osteopathy, massage, physical therapy and midwifery, and of procedural rules and regulations pertaining to the hearing of contested cases before the Minnesota State Board of Medical Examiners.

Copies of the proposed procedural and substantive rules and regulations are available from the Secretary of the Minnesota State Board of Medical Examiners, 230 Lowry Medical Arts Building, Saint Paul, Minnesota, 55102.

Interested persons are invited to attend and submit data or views orally or in writing.

Dated at Saint Paul, Minnesota, this 23rd day of November, 1964.

By Order of the Minnesota Board of Medical Examiners

J. P. Medelman M.D.

Secretary-Treasurer"

Sure, maybe a machine could do your job. But when the boss talks, would it nod and listen? — Changing Times

May we have a minute of your time . . .

We would like your indulgence in filling out the questionnaire which is printed to the right of this article.

It will take only a few minutes. Just fill in the answers, tear off the card, fold it and have your office girl mail it. It is already addressed and stamped for return to us.

Your efforts will help us towards making MINNESOTA MEDICINE a better journal in 1965.

BOARD OF EDITORS
MINNESOTA MEDICINE

President's Letter Continued from Page 61.

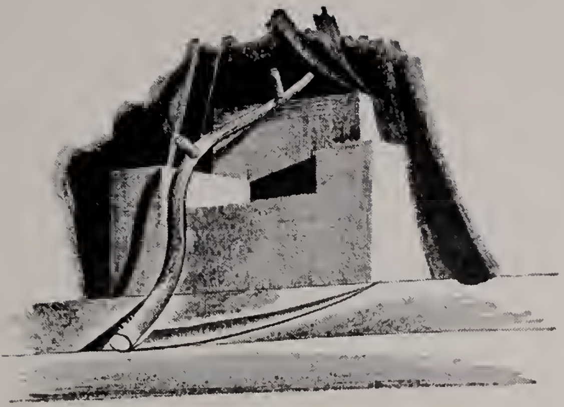
medical family. Many of us practice in rural communities, while others serve in metropolitan areas. When the interests of all are considered, it is apparent that representing the physicians of Minnesota is a responsibility of considerable magnitude. Fortunately, past experience has shown that we work well together, have common interests, and possess an unsurpassed devotion to a high quality of medical care.

The year on which we are entering promises to be replete with the never-ending pressure to keep abreast of scientific advances while we struggle with difficult economic problems in a changing and sometimes critical society. I hope to make the office to which you have elected me representative, useful, and always available.

JMStickney M.D.

J. M. Stickney, M.D.
President
Minnesota State Medical Association

Life is short
Art is long
The occasion instant
Judgment difficult
Experiments perilous—Socrates



In Memoriam

Let death be daily before your eyes, and you will never entertain any abject thought, nor too eagerly covet anything.—Epictetus

HENRY W. WOLTMAN

Dr. Henry W. Woltman, one of the foremost neurologists in the United States and a former member of the Mayo Clinic, died November 27th of cardiac arrest due to calcific aortic stenosis. He was born at Westfield, Wisconsin, and received his doctor of medicine from the University of Minnesota Medical School.

Dr. Woltman was a former president of the Minnesota Society of Neurology and Psychiatry, the Central Neuropsychiatric Association, the Association for Research in Nervous and Mental Diseases and the American Neurological Association. He was a former president of the staff of the Mayo Clinic, a member of the advisory Council of the Neurological Diseases and Blindness Institute, United States Public Health Service and of the Medical Advisory Committee of the National Foundation for Infantile Paralysis. Also, Dr. Woltman was a fellow of the American College of Physicians, the American Academy of Neurology, a member of the American Medical Association, American Psychiatric Association, the Central Society for Clinical Research, Chicago Neurological Association, American Neurological Association, a former chairman of the Section on Nervous and Mental Diseases of the American Medical Association, a member of the Zumbro Valley Medical Society, and a 50 Club and Associate member of the Minnesota State Medical Association.

He is survived by his wife, a daughter and three sons.

LEO A. NASH

Dr. Leo A. Nash, 54, St. Paul radiologist, died December 1st in his home of a heart attack. He was born in Chisholm and received his medical and bachelor's degrees at the University of Minnesota, after which he had a fellowship in radiology at the Mayo clinic.

Dr. Nash was a fellow of the American College of Radiology, a past president of the Minnesota Radiological society and a member of the staff of the clinical institute of the University of Minnesota Medical School. He was a member of the Ramsey County Medical Society, the Minnesota State Medical Association and the American Medical Association.

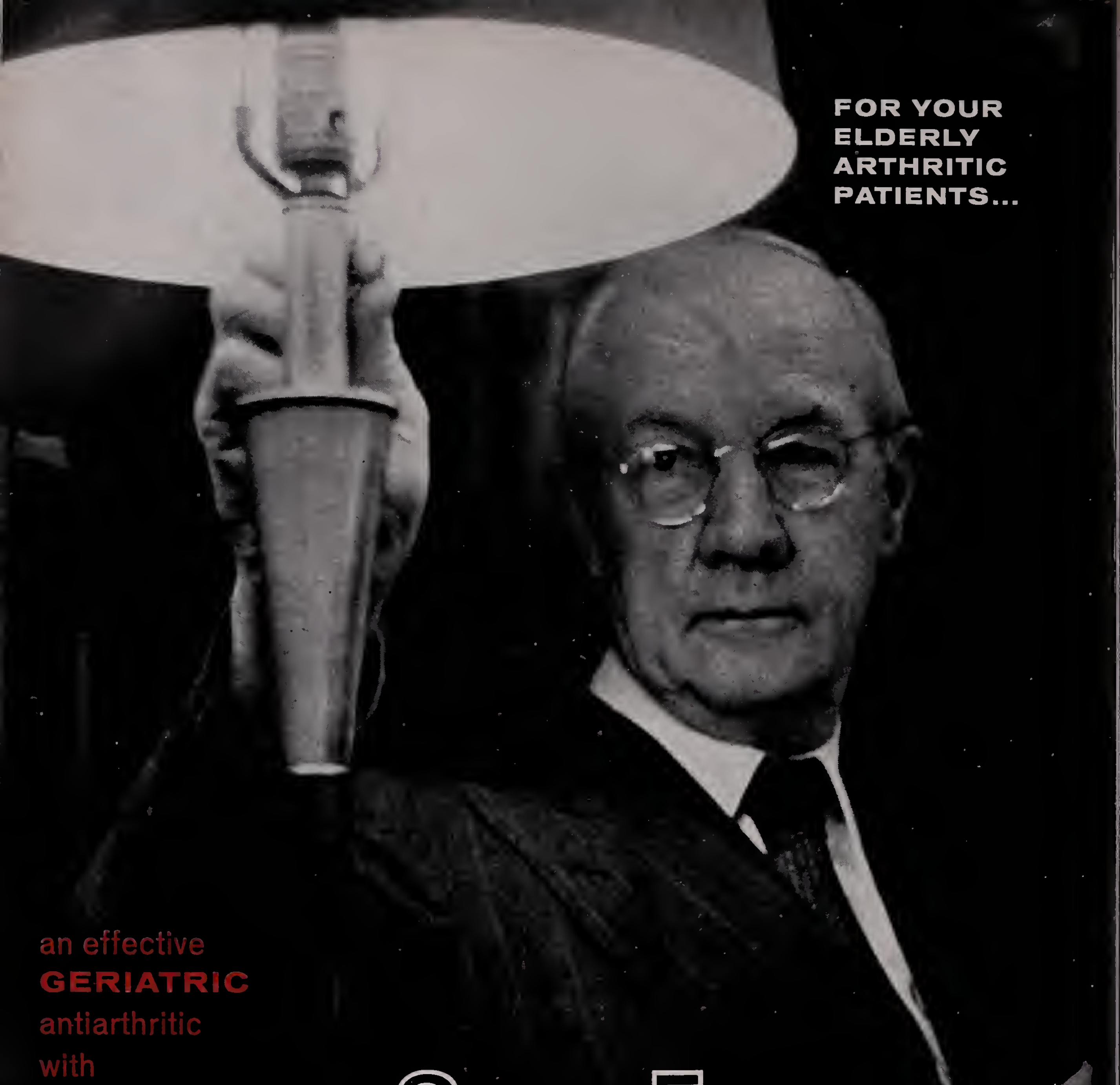
Dr. Nash is survived by his wife, four daughters and a son, Dr. Joel Nash of Albuquerque, New Mexico.

EMIL HABERMAN

Dr. Emil Haberman, 86, Osakis physician, died October 27th. He was born in Waterloo, Wisconsin; however, moved with his parents to South Dakota when he was five years old. He graduated from the University of Illinois School of Medicine, and after a few years went to Osakis where he practiced medicine for forty-three years.

In 1954 the village of Osakis honored his fifty years in the medical profession. He served many years on the Osakis school board of education and was an active member of the Osakis Booster Club and Chamber of Commerce. He was a member of the Stearns-Benton County Medical Society and the American Medical Association and a 50 Club and life member of the Minnesota State Medical Association.

He is survived by his wife, two daughters, and one son, Dr. George Haberman of Baltimore.



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Effectiveness, dependability and reassuring Safety Factors make PABALATE-SF a logical choice for antiarthritic therapy in elderly patients—even when osteoporosis, hypertension, edema, peptic ulcer, cardiac damage, latent chronic infection and other common geriatric conditions are present. The potassium salts of PABALATE-SF cannot contribute to sodium retention...the enteric coating assures gastric tolerance...and clinical experience shows that this preparation does not precipitate the serious reactions often associated with corticosteroids or pyrazolone derivatives.

Side Effects: Occasionally, mild salicylism may occur, but it responds readily to adjustment of dosage. Precaution: In the presence of severe renal impairment, care should be taken to avoid accumulation of salicylate and PABA. Contraindicated: An hypersensitivity to any component.

Also available: PABALATE—when sodium salts are permissible. PABALATE-HC—Pabalate-SF with hydrocortisone.

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In each persian-rose enteric-coated tablet: potassium salicylate 0.3 Gm., potassium aminobenzoate 0.3 Gm., ascorbic acid 50.0 mg.

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Meetings and Announcements

He who knows only his own side of the case, knows little of that.—J. Stuart Mill

JANUARY, 1965

Second Annual American Therapeutic Society-Minnesota Heart Association Symposium, Radisson Hotel, Minneapolis, January 9-10. Subject will be "Therapy of Peripheral Vascular and Cerebral Vascular Disease." Contact: Robert Tuttle, 1821 University Avenue, St. Paul.

Ramsey County Chapter of Minnesota Academy of General Practice, and Ramsey County Medical Society Symposium on "Obesity — Dangers of a Well Fed Population," Lowry Hotel, January 18, in St. Paul. Contact: Charles J. Beck, M.D., 2579 East 7th Avenue, North St. Paul.

St. Louis County Medical Society, Executive Comm. — 6:00 p.m., St. Mary's Hospital, Duluth, January 14. Annual Meeting — 8:00 p.m., St. Mary's Hospital, Duluth.

Ramsey County Medical Society, Lederle Symposium, Lowry Hotel, St. Paul, January 18.

Ramsey County Medical Society, Annual Meeting & Program — 8:00 p.m., 15th Floor Lowry Medical Arts Bldg., St. Paul, January 25.

American Academy of Orthopaedic Surgeons (members and invited guests only), Americana Hotel, New York, January 9-14. Exec. Sec.: John K. Hart, 29 E. Madison, Chicago 2.

Neurosurgical Society of America, The Americana Hotel, San Juan, PR, January 27-31. Sec.: Courtland H. Davis, Jr., M.D., Bowman Gray School of Medicine, Winston-Salem, N. C.

American College of Surgeons (sectional meeting), Atlanta Biltmore Hotel, Atlanta, January 25-27. Sec.: Samuel P. Harbison, M.D., 55 E. Erie, Chicago 11.

Society for Adolescent Psychiatry, New York Academy of Sciences, New York, January 13. Sec.: Frederick J. Wertz, M.D., 30 E. 2nd Ave., New York 10028.

American Academy of General Practice and Mound Park Hospital Foundation, Inc. symposium "Dermatology in General Practice, January 14-16, St. Petersburg, Florida. Contact: Dermatology, Mound Park Foundation, Inc., St. Petersburg, Florida.

Southern Radiological Conference, Grand Hotel, Point Clear, Ala., January 29-31. Sec.-Treas.: Marshall Eskridge, M.D., P.O. Box 4097, Mobile, Ala.

Eleventh Annual General Practice Review, January 17-23, Postgraduate School, University of Colorado School of Medicine, Denver, Colorado. Write University.

FEBRUARY

Minnesota Academy of Medicine, Regular meeting — February 10, 7:00 p.m., Town and Country Club, St. Paul.

St. Louis County Medical Society, Executive Comm. — February 11, 6:00 p.m., St. Luke's Hospital, Duluth. Regular meeting at 8:00 p.m.

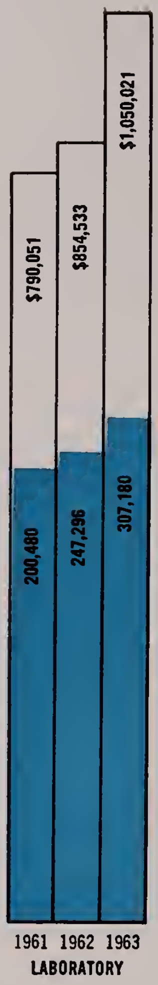
Ramsey County Medical Society, (Business & Program — February 22, 8:00 p.m., 15th Floor Lowry Medical Arts Building, St. Paul.

70th Sioux Valley Medical Association Meeting, February 18 and 19, Sioux City, Iowa at the St. Vincent Hospital and Sheraton Warrior Hotel. Contact: H. E. Rudesdorf, M.D., 2417 Pierce Street, Sioux City, Iowa.

ANNOUNCEMENTS

Applications for the Part I (written) examination to be given on July 2, 1965, will be accepted in the office of the Secretary during the months of January and February. All applications postmarked after February 28th will be returned to the sender. Application forms and Bulletins of the Board may be obtained by writing to the office of the Secretary, — Clyde L. Randall, M.D., American Board of Obstetrics and Gynecology, 100 Meadow Road, Buffalo, New York 14216.

The 28th annual meeting of the New Orleans Graduate Medical Assembly will be held March 8-11, at the Roosevelt Hotel. Details of the New Orleans meeting are available at the office of the Assembly, 1430 Tulane Avenue, New Orleans, La. 70112.



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Yes, Blue Shield wants to serve Minnesota doctors even better than it has.

In 1963 Blue Shield paid for nearly 60,000 more laboratory services than it did in 1962. In dollars this was an increase of over $195,000.

If claims for laboratory services are submitted individually, and if they are paid individually, the cost to Blue Shield increases and the service to doctors suffers.

Collect your laboratory claims and submit them twice (preferrably once) a month. You will be paid promptly, and Blue Shield can operate more efficiently.

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Photographic Contest

The Editors of MINNESOTA MEDICINE, in collaboration with the Doctors' Photographic Society of Minneapolis, take pleasure in announcing a monthly photographic contest. The contest is to promote an interest in photography in the medical profession. First prize each month will be publication in full color of the winning picture in MINNESOTA MEDICINE.

The following rules will govern the conduct of the contest:

1. Only doctors of medicine are eligible to submit pictures, and the picture must have been taken or composed by a physician.
2. Each contestant may submit not more than two pictures each month.
3. Only color transparencies, 35 mm. to 2¼″ can be considered.
4. Each slide should be labeled with the marker's name, address, and the identifying title.
5. Slides should not be mounted in glass, but can be protected in plastic sleeves or envelopes.
6. Each entry must be accompanied by a self-addressed, stamped envelope if return of the picture is desired. Returns will be made shortly after the close of the contest each month. The winning photograph will be retained but will be returned after it has been used.
7. The deadline date for entry will be the 10th of each month and the winner of each month's contest will be announced in MINNESOTA MEDICINE in the subsequent issue. The date of publication will be three to six months in advance.
8. There will be no limitation on subject material except as indicated in item 10.
9. Model releases will be requested of winners where appropriate.
10. Judges will be selected by the editors of MINNESOTA MEDICINE and the Doctors' Photographic Society. The judges will be guided by the precepts of the Photographic Society of America, and winners will be based on appropriateness, interest, impact, and technical excellence.
11. The editors of MINNESOTA MEDICINE and the Doctors' Photographic Society cannot be responsible for entries lost or damaged, but every effort will be made to protect submitted pictures.

Your pictures are hereby invited. Please submit pictures to:

Photo Contest Editor
Minnesota Medicine

Of 507 patients with confirmed ear, nose and throat infections... 465 or 91.7% were treated successfully with Signemycin®

Note:
Adams,* whose 50 patients included 20 with ENT infections, stated that Signemycin "was particularly valuable in infections that did not respond to other antimicrobial agents, and in patients to whom penicillin could not be given." All his cases responded within five days; in most patients, all signs of infection disappeared in three days.

*Adams, J.: J. Tenn. Med. Ass. 50:446, Nov., 1957.

Condition	No. of Patients	No. Responded To Signemycin
Otitis media	90	86
Pharyngitis and laryngitis	162	148
Sinusitis	68	55
Tonsillitis and peritonsillitis	163	153
Various	24	23
Totals	507	465 (91.7%)

consistently effective...often when others fail

Signemycin®

tetracycline HCl, 167 mg.; oleandomycin as triacetyloleandomycin, 83 mg. capsules (250 mg.)

Also available as Syrup, Pediatric Drops, and half-strength Capsules

Brief Summary and Bibliography follow.

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History of Medicine

Andreas Vesalius

Founder of Modern Anatomy

Andreas Vesalius — pioneer, iconoclast, and "heretic" — was born a Belgian into the intolerant and dogmatic 16th century with its inflexible authoritarianism in the fields of science and religion. From early youth the study and demonstration of human anatomy was Vesalius' one passionate pursuit and purpose.

After studying medicine at Paris Vesalius went to Italy to lecture on anatomy at Padua, Pisa, and Bologna — all the while persisting in the dangerous and difficult practice of surreptitiously dissecting human cadavers, whenever available, in order to disprove Galen's erroneous theories of anatomy based on the dissection of lower animals.

Under the odium and stigma of iconoclasm and heresy Vesalius finally felt obliged to leave Italy; bequeathing his lectureship to his pupil Fallopius (of Fallopian tube fame), he went to France and later to Spain to act as court physician to Charles V and Philip II. But the sinister shadow of heresy for presuming to discredit and defy tradition pursued him, and in Spain he was tried by the Inquisition and condemned to death — like his predecessor Servetus, who had been burned at the stake for his numerous heterodoxies, such as maintaining that the blood passes from one side of the heart to the other side by way of the lungs rather than by osmosis, as Galenic medicine had established.

Vesalius' death sentence, however, was commuted on condition he make a devout pilgrimage to the Holy Land, which he did.

In the meantime the atmosphere in Italy was becoming more favorable to Vesalius' "revolutionary" theories and more conducive to such unorthodox practices as human corpse dissection, and Vesalius was invited back to Padua to resume his work there. But on the return voyage — through one of Fate's ironical whimsies — the shop was wrecked and Vesalius perished of starvation and exposure on the Island of Zante, thus depriving the world of the further potential of a brilliant and fearless mind.

Vesalius' "heresy" to medicine consisted in his deposing Galen as the sacrosanct authority in anatomy; His "heresy" to the Church consisted in his "impious" dissection of human bodies, thus making materially intact "resurrection" difficult — to say the least!

Because of Vesalius' iconoclasm: "The four abdominal muscles of the ape no longer graced man; the multi-lobed liver passed away, and so, too, did the segmented sternum, the double bile duct, and the horned uterus. With Galenic error went many ancient anatomical superstitions; the bone Luz, or the resurrection bone, was proved a myth, and Adam's missing rib was restored."*

Vesalius' distinguished work, "De Humani Corporis Fabrica," ranks as one of the great books of the 16th century.

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*Haggard, Howard W., M.D.: "Devils, Drugs, and Doctors," page 147.

Cats are living longer than ever, which proves it can be done without taking up a hobby, joining a club or buying more insurance.—Changing Times

Of 1,028 patients with confirmed respiratory infections... 954 or 92.8% were treated successfully with Signemycin®

Note:
Hammerl* selected his patients for treatment with Signemycin on the basis of demonstrated bacteriological resistance to other antibiotics or failure of previous therapy. Of 100 patients with various respiratory tract infections, 95 responded to Signemycin. Pathogens isolated included staphylococci and *Diplococcus pneumoniae.*

*Hammerl, H.: Wien. Med. Wschr. 108:629, July 26, 1958.

Condition	No. of Patients	No. Responded To Signemycin
Abscess, pulmonary	17	16
Bronchiectasis	19	13
Bronchitis	286	267
Bronchopneumonia	192	179
Empyema	12	11
Pneumonia, lobar	150	146
Pneumonia, other febrile	160	150
Various infected pneumopathies	192	172
Totals	1,028	954 (92.8%)

consistently effective...often when others fail

Signemycin®

tetracycline HCl, 167 mg.; oleandomycin as triacetyloleandomycin, 83 mg.

capsules (250 mg.)

Also available as Syrup, Pediatric Drops, and half-strength Capsules

Brief Summary and Bibliography follow.

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Physician's Diary

No company is preferable to bad, because we are more apt to catch the vices of others than their virtues, as disease is far more contagious than health.—Colton

Dr. E. J. Tanquist, Sr. of Alexandria was honored at a dinner and presented with a plaque by the Kiwanis Club in recognition of outstanding service and leadership to the community.

* * *

Dr. Collin S. MacCarty, head of the section of neurologic surgery of the Mayo Clinic, was chosen president-elect of the staff of the Mayo Clinic at its annual meeting in November. Dr. MacCarty will take office in November, 1965. Dr. Howard P. Rome, senior consultant in psychiatry, who was named president-elect last year, assumed office this year.

* * *

Dr. H. Mead Cavert, assistant dean of the Medical School and University of Minnesota heart researcher, received an $85,000 grant from the Minnesota Heart Association to continue his research.

* * *

A plaque honoring the late Dr. **John M. Waugh**, a Mayo Clinic surgeon, was placed on the sixth floor of the Mayo Building by former Mayo graduate school of medicine fellows who served as his assistants. Dr. **Waugh** died in the summer of 1962 of injuries sustained in a traffic accident.

* * *

NEW LOCATIONS: Dr. **John Arnesen** of Owatonna has accepted a position as chief of the medical service at the Rochester State hospital . . . Dr. **T. J. Thompson** of Milaca left for LaPaz, Bolivia, with his family where they will be serving as medical missionaries in the Pfeiffer Memorial hospital . . . Dr. Reginald G. Bickford of the Mayo Clinic Electroencephalography Laboratories has left the clinic to do research at the Brain Institute, an affiliate of the University of California . . . Dr. **Charles G. Sheppard** of Hutchinson has joined the St. Peter State Hospital staff.

* * *

Dr. R. H. Wilson of Winona has retired from the practice of medicine in that city after thirty-four years of continuous service. Dr. and Mrs. Wilson will continue to live at their home at Queen's Cove, Lamoille, Minnesota.

* * *

Dr. **Joseph M. Janes**, consultant in orthopedic surgery in the Mayo Clinic and professor of orthopedic surgery in the Mayo Graduate School of Medicine, was elected president of the American Automotive Medical Association at its annual meeting.

* * *

Dr. Karl W. Anderson of Minneapolis was elected vice president and Dr. N. L. Gault, Jr., of the University of Minnesota Medical School was re-elected secretary-treasurer of the Minnesota Medical Foundation. The following physicians were elected to the group's board of trustees: Dr. **Dennis J. Kane** and Dr. **William Hartfiel** of St. Paul; Dr. **Cecil J. Watson** and Dr. **Arthur C. Kerkhof** of Minneapolis; and Dr. **Bernard Halper** of Hibbing.

* * *

Dr. Charles A. Neumeister of Edina has been elected to the board of directors of Blue Shield of Minnesota.

* * *

Dr. G. Roy Diessner, a Mayo Clinic consultant, was named president of the Zumbro Valley Medical Society at its meeting in November. Dr. F. Edmund Donoghue of Rochester was elected vice president; Dr. **Malcolm K. Campbell** of Rochester was elected secretary-treasurer, and Dr. **Robert E. Fricke** of Rochester was re-named executive secretary.

Of 1,021 children with various confirmed infections... 950 or 93.0% were treated successfully with Signemycin®

Note:
The effectiveness of Signemycin was demonstrated by Chattas and his co-workers* who administered Signemycin to 30 children with serious staphylococcal infections resistant to commonly used antibiotics. Only one failed to respond. In each case the use of this drug was indicated by antibiogram. Those children treated with a nonselected antibiotic—for comparative purposes—took three times longer to recover.

Chattas, A. et al.: Antibiot. Med. 7:300, May, 1960.

Condition	No. of Patients	No. Responded To Signemycin
Eye, ear, nose, throat infections	368	343
Respiratory infections	369	346
Gastrointestinal infections	42	30
Skin and soft-tissue infections	38	37
Deep-seated or generalized infections	47	44
Various conditions	157	150
Totals	1,021	950 (93.0%)

consistently effective...often when others fail

Signemycin®

tetracycline HCl, 167 mg.; oleandomycin as triacetyloleandomycin, 83 mg.

capsules (250 mg.)

Signemycin is also available as half-strength Capsules, preconstituted raspberry-flavored Syrup and Pediatric Drops

Brief Summary and Bibliography follow.

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Classified advertising rates are twenty (20) cents a word; minimum monthly charge $5.00; key number, fifty (50) cents additional.

Replies to advertisements with key numbers should be mailed in care of MINNESOTA MEDICINE, *496 Lowry Medical Arts Bldg., St. Paul, Minn. 55102*

MORGAN, MINNESOTA, Wants General Practitioner — Present Physician retiring after 33 years. Opportunity to take over well established practice. Progressive community in the best rural area of Southern Minnesota. Office space and equipment available. Call or write John Hageman, Pharmacist, Morgan, Minnesota. Telephone Morgan No. 96.

WANTED LOCUM TENENS — must have Minnesota license. Small town 5,000. Local practice only. Four-six weeks. Salary: $1500-2000. Must be recommended. Write: MINNESOTA MEDICINE, Box 292, 496 Lowry Medical Arts Building, St. Paul, 55102.

PEDIATRICIAN — to head pediatric department of expanding prepaid medical specialty group; Minneapolis-St. Paul; excellent beginning salary; opportunity for teaching and professional pursuits; liberal vacation and benefits. Alfred F. Anderegg, M.D., Medical Director, 2500 Como Avenue, St. Paul 8, Minnesota.

WANTED: General practitioner for Northern Minnesota town. An eight-room clinic located on main street equipped with X ray, etc. Previous practitioner left because of ill health after ten years profitable practice. Golf, hunting and fishing. No initial investment necessary. Write: MINNESOTA MEDICINE, Box 294, 496 Lowry Medical Arts Building, St. Paul, 55102.

BURNSVILLE MEDICAL CENTER — office space for one, two or group of physicians in Twin Cities fastest growing suburb — ideal for second office. Call Minneapolis 890-1434 or St. Paul 698-8618.

WANTED: General practitioner by established three-man group in own building, fully equipped. Southwestern Minnesota — county seat — population 3,500. New hospital — fine churches — good schools, public and parochial. Golf club — grass greens. Hunting and fishing. Starting salary with opportunity for partnership. No initial investment necessary. Write: MINNESOTA MEDICINE, Box 199; 496 Lowry Medical Arts Building, St. Paul 55102

WONDERFUL OPPORTUNITY — Mankato, Minnesota — for a specialist in ENT, OB-GYN and urology in independent practice. Referral practice assured. Office space available. City is 35,000 with trade area of 160,000. Two excellent hospitals with open staff of 60 men, 40 of whom are specialists. Mankato State College enrollment over 8,000 with excellent nursing school. Extremely well-balanced, diversified economy. Write: MINNESOTA MEDICINE, Box 295, 496 Lowry Medical Arts Building, St. Paul, 55102.

WANTED: INTERNIST, board eligible, who is interested in joining a small group in west central Wisconsin. Salary arrangements to start with early partnership. WRITE: MINNESOTA MEDICINE, Box 296, 496 Lowry Medical Arts Building, St. Paul, 55102.

WANTED general practitioner for locum tenens for the month of February, 1965. Modern hospital and clinic, consultation available. Will pay $1,200 for the month. Write or call collect: William C. Heiam, M.D.; Cook, Minnesota.

INTERN ANCKER HOSPITAL, ST. PAUL would like to associate in general practice with established group in Minnesota or Wisconsin. 1964 Graduate Indiana University School of Medicine, 25 years old, married, two children. Available after June 30, 1965. Salary leading to partnership after one year if mutually agreeable. Military obligation completed. Write: Stephan H. Earl, M.D.; Interns Quarters; Ancker Hospital, St. Paul, Minnesota.

PROFESSIONAL AIR AMBULANCE. Multi or single engine aircraft. All weather and night flight capability, anywhere in the U. S. Oxygen, Respirator, Aspirator, Nursing service, all medications. Also full time M.D. Board Anesthesiologist providing all medical care in flight available on request. MIDWEST AIR TRANSPORTS, Operations Office, Municipal Airport, Waterloo, Iowa, Phone 319-2331083.

WANTED: Two general practitioners who are interested in general medicine and obstetrics to associate with a small group in west central Wisconsin. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE, Box 286; 496 Lowry Medical Arts Building; St. Paul, 55102.

MEDICAL CLINIC for two or more doctors on first floor of up-to-date fireproof building at 806 E. 7th Street, St. Paul. Demand for doctors in this vicinity. Telephone: 646-4240 or 644-4567.

HOME NURSING REGISTRY — professional background. RNs, LPN, PNs, nurses aides, companions. Well screened, classified and placed according to qualifications. Garvue Nurses Registry, Minneapolis. Telephone: 926-4495 or 926-4310.

WANTED: Three doctors — Internist, Pediatrician, General Practitioner. Salary for one year then partnership if mutually agreeable. New completely equipped office in Maplewood; 6 year old established practice in Bayport. Call 739-5050 or write Johnson Clinic, 2716 Upper Afton Road, St. Paul 19, Minnesota.

OFFICE AVAILABLE. Corner State and Concord Sts., St. Paul. Four blocks from Riverview Memorial Hospital. Doctor retiring because of health. Rent $65.00 month. The following office fixtures Free: Examining table, scales, Jones Basal Metabolism, Ifra Red, Diathermy, new EKG, desk, air conditioners, etc. Write or call M. D. Hunsaker 176 Concord St., St. Paul, Minn. 55107. Ca7-6922.

PSYCHIATRIC RESIDENCIES: positions available January and July 1965. Fully approved; balanced didactic and clinical experiences. Five-year career program; $8,519, $9,855, $11,525, $14,908, $15,722. In Michigan's Water-Winter Wonderland. Dr. Curtis W. Page, Director of Training, Traverse City State Hospital, Traverse City, Michigan. An equal opportunity employer.

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SIGNEMYCIN®

Side Effects: Glossitis and allergic reactions, as well as severe anaphylactoid reactions, have been reported as rare side effects. Should significant reaction or idiosyncrasy occur, discontinue medication and institute countermeasures. Use of tetracycline during the last trimester of pregnancy, neonatal period and early childhood may cause discoloration of developing teeth. Reduce usual oral dosage and consider serum level determinations in patients with impaired renal function to prevent possible liver toxicity due to excessive accumulation of antibiotic in the serum.

Precautions: Overgrowth of nonsusceptible organisms may occur. In such cases, discontinue medication and institute appropriate specific therapy as indicated by susceptibility testing. Aluminum hydroxide gel given with antibiotics has been shown to decrease their absorption and is contraindicated. The coloring agents used in Signemycin Syrup and Pediatric Drops may produce red discoloration of stools.

Triacetyloleandomycin, a constituent of Signemycin, administered to adults in daily oral doses of 1.0 Gm. (3 Gm. Signemycin) for periods of more than ten days may produce hepatic dysfunction and jaundice. In the rare patient who requires this high dosage level of Signemycin initially, liver function should be carefully followed and dosage should be reduced, as promptly as possible, to the usual recommended range of 1.0 to 2.0 Gm. per day. Therefore, Signemycin is recommended primarily for the treatment of acute or severe infections, with treatment restricted to a ten-day period. If clinical judgment dictates continuation of therapy beyond ten days, serial monitoring of the liver profile should be carried out, including BSP, transaminase, and cephalin flocculation tests. Changes observed in liver function were reversible following discontinuation of the drug.

Formulas: Capsules: 250 mg. Signemycin (167 mg. tetracycline HCl and 83 mg. oleandomycin as triacetyloleandomycin).

Capsules: 125 mg. Signemycin (83 mg. tetracycline HCl and 42 mg. oleandomycin as triacetyloleandomycin).

Syrup: 125 mg. Signemycin (tetracycline equivalent to 83 mg. tetracycline HCl and 42 mg. oleandomycin as triacetyloleandomycin) per 5 cc.

Pediatric Drops: 100 mg. Signemycin (tetracycline equivalent to 67 mg. tetracycline HCl and 33 mg. oleandomycin as triacetyloleandomycin) per cc.

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Note:

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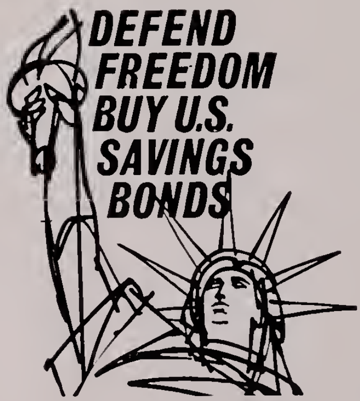

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(1) Frykman, H.M.: Minn. Med., Vol. 38, Jan. 1955. (2) Poth, E.J.: The J.A.M.A., Vol. 163, No. 15, April 13, 1957. (3) McGivney, J.: Texas State Jour. of Med., Vol. 51, No. 1, Jan. 1955. (4) Stern, F. H.: Jour. of The Amer. Ger. Soc., Vol. 11, No. 3, Mar. 1963. (5) Weekes, D. J.: N.Y. State Jour. of Med., Vol. 58, No. 16, Aug. 1958. (6) Abbott, P.L.: Jour. of Oral Surg., Anes. & Hosp. Dental Serv., Vol. 19, July 1961. (7) Weekes, D. J.: E.E.N.T. Digest, Vol. 25, No. 12, Dec. 1963.

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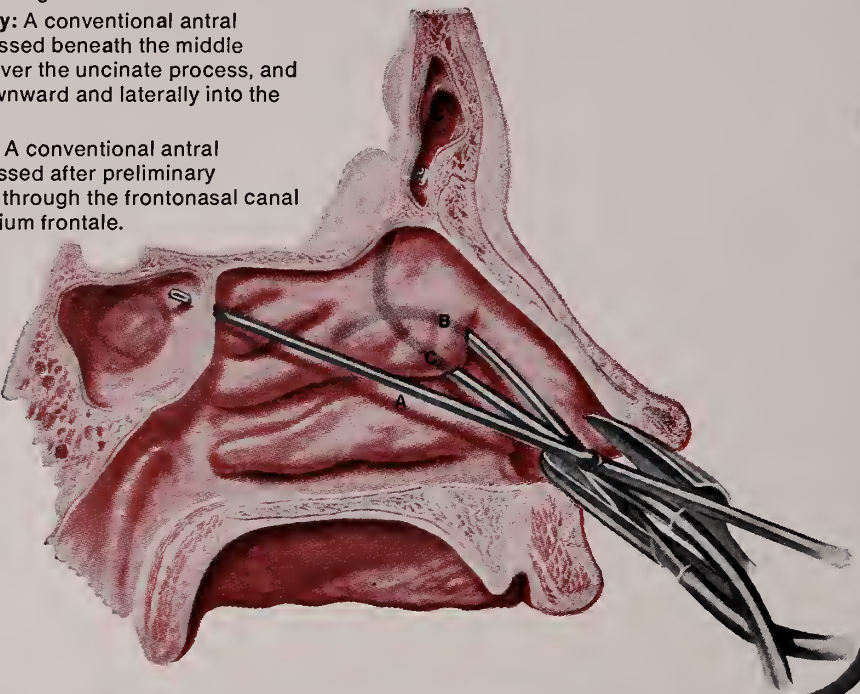

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*Reed, G. F.: Sinusitis, New England J. Med. 267:402, Aug. 23, 1962.

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President's Letter

It is apparent to the physician who reads the current literature on medical economic problems that the cost of health care is of great concern to the American public and its elected representatives in government at all levels. The most rapidly rising factor is the cost of hospital care, which now amounts to more than a third of the total cost. Those who have to do with hospital care naturally concern themselves with all phases of this cost. Efficient use and location of hospital facilities are imperative if costs are to be controlled. Therefore, the adequate planning of hospital construction in geographic areas large enough to be effective is most important.

The American Medical Association has made its position on area-wide hospital planning clear in a series of resolutions passed by the House of Delegates in the years 1962, 1963 and 1964. State and county medical societies and individual physicians are encouraged to participate in the formation and operation of regional hospital-planning bodies under a voluntary system. The dangers inherent in enabling legislation, which would establish a compulsory system, are emphasized. The recently enacted Metcalf-McCloskey Bill in New York is an example of such legislation.

Under the Hill-Burton Act there are funds available for the establishment of planning agencies at state and county levels. This act has served as a stimulus, so that communities in which planning agencies have functioned now contain about 40 per cent of the nation's physicians. These communities are, for the most part, in urban centers. In Minnesota there are planning councils in Minneapolis, St. Paul and Duluth which are operating by means of grants from the Public Health Service to the State Department of Health. These grants are about to expire. The Minnesota Hospital Association is proposing the creation of a state-wide planning committee and has invited the Minnesota State Medical Association to share the responsibility jointly with it and with the State Board of Health. In the past the State Board of Health, as a result of its administration of Hill-Burton funds and its licensing power, has been the major element in the planning and approval of hospital facilities. The proposal of the Minnesota Hospital Association is welcomed by the State Board of Health because it adds the desirable element of representation from the medical and hospital professions. The Minnesota Hospital Association also proposes to join with the Minnesota State Medical Association to assist in the establishment of voluntary local and area-wide planning councils for hospitals and related health facilities. In addition, the activities of established planning agencies would be coordinated. At its December meeting the council of the Minnesota State Medical Association approved such action for a year's trial, and referred the plan to the Committee on Hospital and Professional Relationships for development.

With the full approval of the American Medical Association, the American Hospital Association and influential business leaders, there seems little doubt that area-wide hospital planning will proceed. Physicians must be a major force in working with responsible

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Radiation in Pregnancy*

KARL K. LATTEIER, M.D.**
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Detroit, Michigan

A FEW years ago, when fallout from atomic tests triggered a radiation scare, the danger of radiation in pregnancy became so exaggerated that the use of X-ray diagnosis was temporarily abandoned by many doctors. However, it was soon discovered that X-ray examination was necessary to maintain obstetrical standards and to prevent fetal loss and maternal complications.

The widespread publicity of radiation dangers, however nebulous they may be, has served a good purpose. It has united the medical professions and allied agencies to develop a high standard of radiation protection. It has stimulated enactment of laws prohibiting dangerous and unwarranted lay use of radiation. Manufacturers have developed safer and more effective shielding for X-ray equipment. Manufacturers of films have developed high-speed film and cassettes with improved developing technique reducing X-ray exposure. Today radiation is a valued diagnostic tool, essential to modern medical practices. Indirectly it saves innumerable lives daily, through its diagnostic and therapeutic application.

Today the use of medical radiation is increasing. The expansion in hospital construction and facilities has increased the availability of radiological facilities to patients. There has also been greater insurance coverage for radiological examination. Further, the advance in medical science has opened new fields of radiation diagnosis and treatment. The technique which enables the radiologist to visualize the blood vessels in almost any part of the body by the introduction of a contrast medium is becoming commonplace even in small hospitals away from the medical centers. Radioactive isotopes can be introduced into the body by vein or through the intestinal tract, systematically traced to various parts of the body, and their absorption and excretion accurately calculated. Additional physicians are continually being licensed to use isotopes. Isotope labs are no longer limited to hospital radiological departments but are now available in offices and clinics.

Such new applications of radiation have already been used in the care of the pregnant patient. For example: placental visualization which was formerly a complicated film study can now be easily demonstrated by a single X-ray film, by isotope radiation studies, by aortography, and by injection of contrast media into the amniotic sac. However, the additional stress of pregnancy may aggravate pre-existing heart, thyroid, lung, kidney or intestinal diseases, requiring additional radiation studies. It is important, therefore, to use radiation sparingly, selecting it only for the most urgent needs throughout the pregnancy. Let us curtail our enthusiasm for diagnostic radiation procedures having only an academic interest, and let us limit their use to physicians with sufficient interest in their profession to maintain adequate safe guards.

---

*Presented at the Minnesota State Medical Association Annual Meeting in Rochester, May 19, 1964.

**Department of Radiology, Crittenton Hospital of Detroit.

***Department of Obstetrics and Gynecology, Crittenton Hospital of Detroit.

Currently a survey is being conducted jointly by the division of Radiological Health and the National Health Survey under the auspices of the United States Public Health Service. The object is to eliminate unnecessary radiation exposure, but may actually result in restrictions in medical use of radiation. If we wish to keep radiation protection and control under medical supervision and prevent unwarranted or unreasonable government control, we must avoid all unnecessary radiation in any form.

How Safe and How Harmful is Radiation in Pregnancy?

Radiation, like drugs, foods, or anything else, is dangerous if you get too much of it. Therefore the most obvious method of protection must be by measuring and limiting its use. Radiation disrupts molecules, thereby injuring cell function; this may be desirable in therapy, but obviously is not for use in diagnosis.

Everyone is aware of the hazards of large amounts of radiation, but we do not know the effects of small doses. We state that there are somatic and genetic hazards as a result of radiation in small amounts and to limited portions of the body. In theory and from insect and animal experimentation the greatest genetic effect appears to be the addition of undesirable mutants through radiation exposure of the gonads. This effect is thought to be cumulative, and there appears to be no threshold below which radiation can be considered safe. Now this involves the segment of the population including both the mother and the fetus. Therefore, much objection to radiation in pregnancy is derived from this source.

The Somatic Hazard

Since the radiation effect is disruption of the molecules, even a diagnostic X-ray procedure must produce some cell damage. Diagnostic exposures may vary from a few milliroentgens to several roentgens. However, the somatic effect may be limited by a threshold below which radiation injury to the cell is sublethal and partial or total cell recovery occurs. This threshold in humans is still unknown; but it has been learned from rodent and other animal experimentations that as little as twenty-five rads absorbed by the developing embryo at its most sensitive stage, from conception to three months, may produce malformations. No developmental change can be produced by radiation, however, after a period of six weeks gestation, because by that time all of the organ systems have formed. Larger amounts of radiation are then required to produce an undesirable effect.

We must remember that during the entire pregnancy, radiation of the mother's abdomen constitutes whole body radiation of the fetus, and during the first trimester embryonic tissues show an increased cell sensitivity at least double or possibly three or four times that of the mother. Another question arises as to whether or not diagnostic studies during pregnancy increase the incidence of neoplasm, especially leukemia, in the offspring. Statistical evidence has been presented to support the contention that no neoplastic increase or carcinogenesis is attributable to diagnostic radiation. Large studies, especially the report which surveyed nearly 40,000 individuals who had been subjected to diagnostic X ray while in utero showed that the incidence of leukemia was not greater than that in the general population.

What Can We Do to Protect the Pregnancy?

Elective X-ray Examination During the Menstrual Period

The general use of roentgen examination as a diagnostic study apart from pregnancy with inadvertent radiation in early pregnancy before it is recognized by the patient or by the physician may constitute the greatest hazard of radiation in pregnancy; this hazard, however, can be largely eliminated by having such elective radiological examinations, especially when fluoroscopy or multiple exposures are involved, made during the menstrual period or the ensuing two weeks.

Avoid Radioactive Isotopes

It is our policy to avoid the use of radioactive isotopes in treatment or diagnosis of hyperthyroidism during pregnancy, since in early pregnancy it is undesirable from the standpoint of the sensitivity of the fetus, and in later pregnancy it is undesirable due to the fact that the fetal thyroid may concentrate and retain radioactive iodine which could result in a hypothyroid fetus.

Use Semi-opaque Plastic Filter

In the later part of pregnancy, especially in the last trimester, total body irradiation of the fetus may be minimized by the use of semi-opaque plastic filters shaped to avoid over-exposure of the thin part and reduce the amount of radiation, yet still allow sharp definition of the cleavage planes permitting visualization of the urinary bladder, placenta, and bone structures of the pelvis with one film exposure of much less than an average absorbed radiation dose. The filters prevent the soft rays, which do not aid in exposure of the film, from entering the tissues. Grossly over-exposed film or a retake study destroys the value of low dosage technique; improper positioning and other technical factors reducing diagnostic accuracy are to be avoided by certainty that work is done by competent personnel.

What are Considered to be Justifiable Roentgen Studies During Pregnancy?

In many states the premarital examination is required by law, and we should use this opportunity to examine our patients thoroughly. The premarital examination also offers an excellent opportunity for the doctor to acquaint his patient with the medical concepts of radiation in pregnancy and to advise the patient to have routine chest study and radiological investigation of urinary or gastrointestinal tract, if indicated, prior to conception.

Avoid X ray During First Trimester

At the patient's first prenatal visit, a chest film is not necessary. This is especially true if she presents herself for care in the first trimester. Initially, a tuberculin test can be made. Chest X rays are then indicated on the positive reactor. We prefer a large chest film to a photofluorogram which requires four to 10 times as much exposure and is less reliable. Also, no permanent record results if only a photofluorogram is used. Radiological work-up of other problems found in the first prenatal visit can usually be postponed until after delivery or at least until the second or third trimester. Gastrointestinal and urologic studies are especially to be avoided, and it is not necessary to subject the patient to radiation merely because of pyelitis. With suspicion of malignancy, roentgen study is probably justified. Fortunately it is rare in this age group.

Threatened abortion is perhaps the most common problem in the first trimester, but here again X ray is of no use. In the question of *ectopic pregnancy,* radiologic methods, with the exception of arteriography, have not been reliable. Culdocentesis and culdoscopy appear safer and are more accurate. In cases where *hydatiform mole* is suspected, serial gonadotropic assay is done to establish the diagnosis. Here roentgen studies are usually helpful only after the pregnancy is of four to six months' duration; even then the presence of a fetus may confuse the issue, as a mole can co-exist with a fetus.

X ray During Second Trimester

Hydramnios should certainly be investigated, as fetal anomaly is often responsible and easily found by roentgen study. Abdominal pregnancy is rare; to be certain, however, the diagnosis may be lifesaving. Film studies are helpful especially if a sound or contrast medium is placed in the uterus, as the abdominal gestation can then be clearly demonstrated. *Multiple pregnancy* in the second or third trimester can be easily diagnosed by a single film exposure. Second trimester *intrauterine fetal death* can usually be diagnosed by clinical means and fetal electrocardiography, but Roentgen confirmation in five to seven days after death is helpful and quite accurate. It may support a clinical diagnosis of fetal death even earlier.

X ray During Third Trimester

The etiology of bleeding in the second trimester is very difficult to diagnose by routine radiologic studies. It is probably in this area that special studies such as *arteriography and isotope studies* will prove more valuable. It is indeed fortunate that the radiologic studies in pregnancy are most valuable and accurate in that portion of pregnancy where they are the safest, namely, in the third trimester. Certainly previously mentioned conditions such as hydramnios, multiple pregnancy, fetal death, and abdominal pregnancy may first be suspected or diagnosed in the third trimester.

Pelvimetry is most valuable if done on the patient when she is in labor. Roentgenograms using a standing film can readily be taken during labor. In reviewing our staff cases we find that less than half of the patients where dystocia is suspected by clinical means, will actually require pelvimetry, provided one waits for the onset of labor before ordering the films. Certainly if difficult or mid-forceps delivery is contemplated, the forceps can be applied more intelligently if the fetal position and pelvic architecture are known. When a patient in labor stops making progress, the diagnosis of inertia cannot be made until disproportion is ruled out. Pitocin is a great aid in the management of inertia but may be a great tragedy in disproportion. This is certainly true in a primigravida or even in a multipara who may have delivered a small baby but cannot deliver the larger fetus.

In early labor, pelvimetry is indicated to explain *the unengaged head,* especially in a primigravida, and also in the primigravida breech. However, roentgen examination in all breech presentations prior to term is not indicated, since spontaneous conversion to vertex is common.

Placentography in the third trimester may eliminate the need for a double set-up for management of *uterine bleeding near term.* The double set-up in itself may force one's hand to an immediate cesarean section, even with a grossly premature fetus. X ray offers an accurate and safe way to make the diagnosis without the risk of hemorrhage. Since the initial bleeding is usually not severe, we are able to treat the patient expectantly and perhaps gain two or three weeks of additional intrauterine life for the fetus, or an increase of six to eight ounces in weight, by keeping the mother at bed rest and prepared for emergency surgery. *When a patient bleeds in the last trimester the differentiation between placental separation and placenta previa must always be made.* Prolonging intrauterine life in placental separation may induce fetal death. Usually the diagnosis can be made accurately on the basis of a single lateral film. If placenta previa is not present, the diagnosis is most commonly abrupto or marginal sinus separation. Then a vaginal examination can be done and the mode of delivery decided upon, based on the status of the fetus, the status of the cervix, and the convictions of the obstetrician involved. It is our feeling that placentography is more valuable than isotope studies in evaluation of placental location at term. The isotope studies locate the placenta as to whether it is on the right or on the left, but this is probably of very little clinical significance. The other advantage of placentography at term lies in the additional information that we can derive, such as the position and maturity of the fetus, and whether or not there are any congenital abnormalities present.

Should Routine Films for Fetal Age and Size Be Done?

There is no point in doing routine films long before term, as they will only have to be repeated. If the obstetrician plans a cesarean section at 38 to 40 weeks, he should have roentgen consultation only if he is concerned about the fetal size or length of gestation. In a recent review of our cesarean sections, we have found no prematures resulting from scheduled repeat sections at 38 to 40 weeks even though no radiological studies were made. Obviously, if a cesarean section is to be done prior to term for diabetes, toxemia, or Rh incompatability, a film for fetal age and size is of great value.

Discussion

There seems little doubt that modern diagnostic radiology used intelligently in the obstetrical care of patients can keep alive mothers and babies who otherwise would die. Practically, we have no personal knowledge of neoplasm or fetal malformation resulting from the use of diagnostic roentgen procedures in our practice. We are certain that we have saved both mothers and infants by judicious and carefully applied roentgen studies of high technical quality. It is a mistake to allow the technician who is not well versed in technique to utilize this procedure, and it behooves the radiologist and the obstetrician to learn as much about these subjects as possible in order to obtain the maximum amount of information from each film.

Those of you who can remember birth injuries realize that a fetus damaged as the result of trauma sustained during delivery is a burden on society and the immediate family greater than the radiation danger in any form. Markedly prolonged labors that have been terminated by difficult forceps deliveries have largely disappeared. Surely cesarean section is an entirely safe procedure and the indication for cesarean section is frequently determined by the roentgen study. There are usually no contraindications to a trial labor if it seems desirable, but even this might be avoided by proper roentgen examination. A single lateral view at approximately 36 weeks of gestation in repeat sections makes it possible to increase the over-all birth weight by eliminating prematurity in elective section. With the use of X ray it is possible to avoid section in instances of fetal malformation, and fetal death can be diagnosed before the clinician is aware of this complication.

Summary

One of the greatest hazards of radiation in pregnancy can be eliminated by conducting extensive elective radiological examinations during the menstrual period and the ensuing two weeks. During pregnancy, the management of the prenatal period and labor may be safely conducted, using radiological procedures as necessary when radiation control and protection assure the safety of the mother and fetus. The need for each radiological examination should be carefully evaluated.

No specific procedure can be condemned if it is sufficiently indicated for the good of the mother or the infant.

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ABDOMINAL MIGRAINE SYNDROME

Abdominal pain, nausea, vomiting, and occasional diarrhea are occasionally a conspicuous part of the clinical picture of migraine headache. This has been principally seen in children or young adults who have had migraine headaches for years.

The parenteral administration of ergotamine usually causes prompt subsidence of the symptoms. Desensitization with intravenous histamine has been found to provide prolonged relief.

Durham-Encyclopedia of Medical Syndromes
Hoeber, Inc., New York

Protect the birds. The dove brings peace and the stork brings tax exemptions.

Evaluation of a New Bronchographic Medium

Ever since 1922, when Sicard and Forestier[1] introduced the use of iodized peanut oil in clinical bronchography, clinicians have sought the ideal bronchographic medium. In order for a material to qualify as a good substance for use in bronchography, it must (1) be sufficiently radiopaque to provide good contrast on thoracic roentgenograms, (2) be able to coat the inner surface of the bronchial tree so that good anatomic detail can be delineated on roentgenographic examination, (3) be nonirritating to the respiratory tract, (4) be easily and quickly eliminated from the lungs, and (5) be incapable of producing either transitory or permanent toxic changes in the lungs.

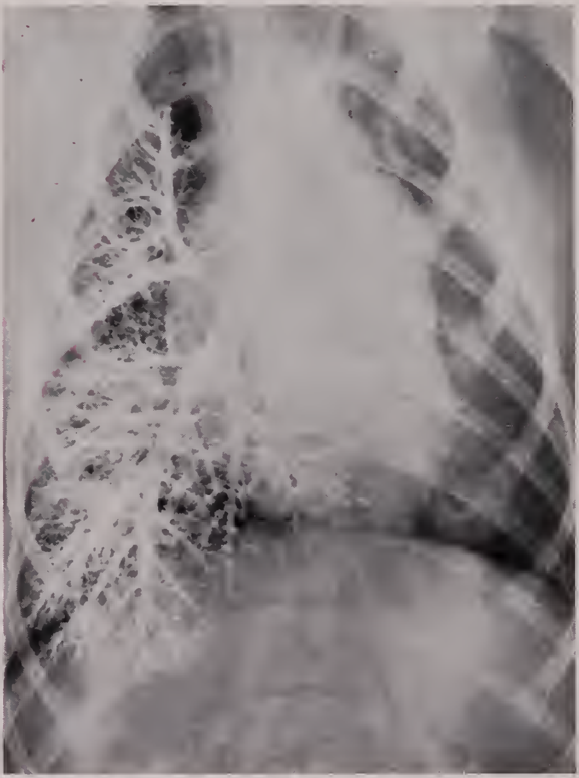

Fig. 1 *(a)* — Contrast produced by medium studied.

Much has been written concerning the efficacy of various media used in bronchography. We recently have encountered a medium which renders excellent bronchial detail on roentgenograms and, therefore, undertook a study of its potential toxicity. We think that any new medium should be thoroughly studied for possible untoward reactions, and we would like to discuss a method that we employed in evaluating such a medium.

Methods

Five mongrel dogs were anesthetized lightly with thiopental (Pentothal), and a tracheal catheter was inserted in each dog. In four animals, 5 ml. of a water-soluble bronchographic medium was instilled into the right side of the bronchial tree. In the other dog, 5 ml. of an oil-base medium (propyliodone [Dionosil]) was used in the same manner.

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An Experimental Study

Anteroposterior bronchograms were made, the dogs were placed in a head-down position to allow the media to drain from the lungs, and the animals were allowed to recover from the anesthetic. Roentgenograms were made the next morning for evidence of retained material.

One animal was sacrificed two days and one six weeks after bronchography. Two animals had right lower lobectomy 48 hours after bronchography. One of these was necropsied 10 days after operation, and the other, six months later. The animal exposed to the oil-base medium was sacrificed two days after bronchography.

In each case, the lungs were examined for the presence of foreign material, and sections of tissue from the basal segments and from the superior segment of the lower lobe were stained with hematoxylin and eosin. Fresh-frozen sections were stained for fat and were examined microscopically. Each section was examined under polarized light for evidence of retained material.

Results

All animals survived the bronchographic procedure. Of the two dogs subjected to right lower lobectomy, one survived and was sacrificed six months later; the other grew lethargic seven days postoperatively, became febrile, and died on the tenth postoperative day.

The bronchographic detail made possible by the new medium is illustrated in Figure 1*a*. The outline of the bronchial tree is considered to be somewhat superior to that obtained by the use of the oil-base medium (Fig. 1*b*).

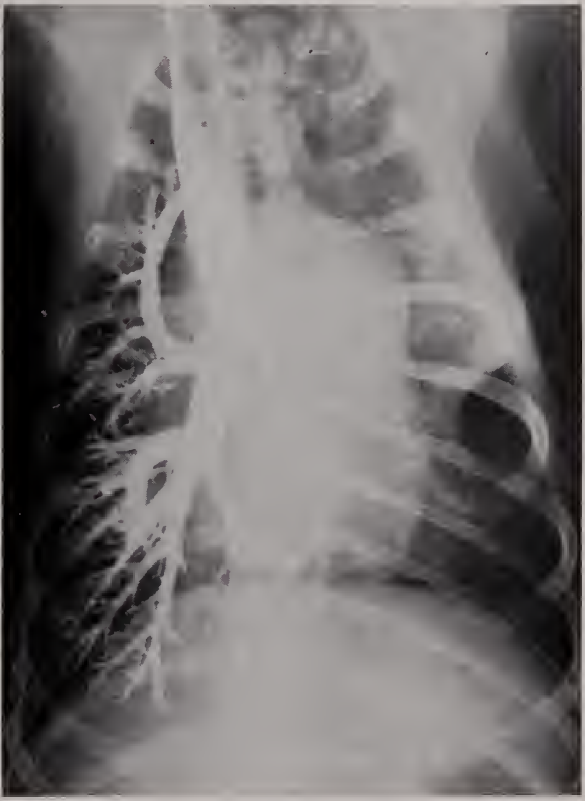

Fig. 1 *(b)* — Contrast produced by oil-base medium.

Roentgenographic Findings 24 Hours After Bronchography

Of the four animals exposed to the new medium, only one showed evidence of retained medium in the lungs the next morning (Fig. 2), and it was this animal that died 10 days after lobectomy, apparently of pneumonia and empyema. The animal exposed to the oil-base medium did not have demonstrable radiopaque material in its lung 48 hours after bronchography.

Pathologic Findings

Forty-eight hours after bronchography examination of the lower lobe of the right lung showed medium to be present both grossly and microscopically in one of three animals examined. The heaviest concentration was seen in the basal segments of the lower lobe, with moderate amounts in the superior segment. The material was found to be doubly refractile on microscopic examination and could be identified easily when viewed with polarized light. Numerous particles of medium were identified microscopically in the bronchi of the lower lobe and in a hilar node removed at the time of operation (Fig. 3). Associated with the deposition of medium within the lung was a moderately severe inflammatory reaction, particularly marked in the peribronchial regions (Fig. 4). The two other animals examined at this time did not show evidence of retained medium either grossly or microscopically, but microscopic examination of tissue from the basal segments and superior segment showed responses that varied from mild inflammation and atelectasis to patchy pneumonitis and bronchopneumonia (Fig. 5). Associated with the pneumonic change was some hyperplasia of bronchiolar epithelium (Fig. 5*b*). The irritative effect was evident predominantly within and around terminal bronchioles and alveolar ducts rather than in relation to the larger bronchi (Fig 5*a* and *b*). The lung of the dog exposed to the oil-base medium and sacrificed two days later showed no gross abnormality, and little or no inflammatory reaction could be demonstrated microscopically.

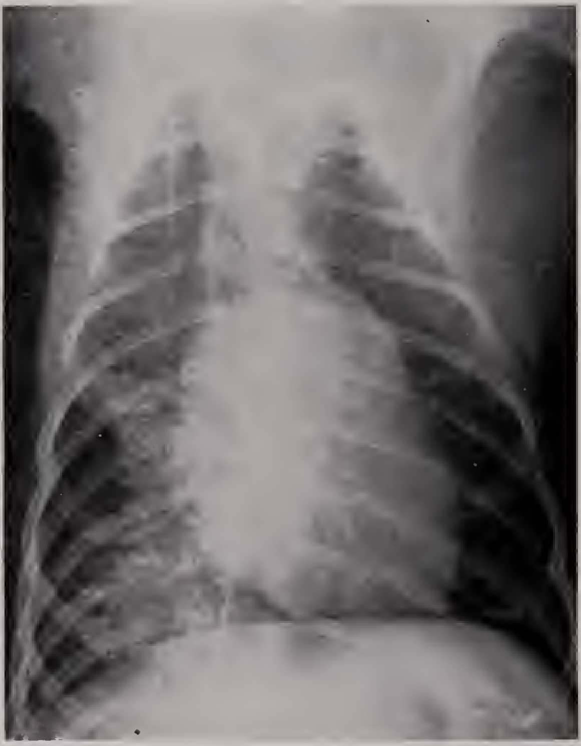

Fig. 2 — Roentgenogram taken 24 hours after bronchography showing retention of medium in the right lung.

At 12 Days After Bronchography.

Examination of the left lung and the remaining part of the right lung of the dog that died 10 days after lobectomy revealed that the cause of death was undoubtedly a fulminating pneumonia. The right pleural space was filled with purulent exudate, the right lung was hyperemic and heavy, and purulent material could be expressed from the parenchyma. The left lung also was involved in the inflammatory process. Microscopically, medium could be seen in the parenchyma and in some of the larger bronchi. The inflammatory reaction was intense and was associated, in many regions, with deposits of bronchographic medium.

At Six Weeks After Bronchography

No medium could be identified on gross or microscopic examination of the lung at this time. Some residual inflammatory reaction was noted, predominantly peribronchial in distribution (Fig. 6).

At Six Months After Bronchography

No gross changes were present in the remaining lung tissue. No medium could be

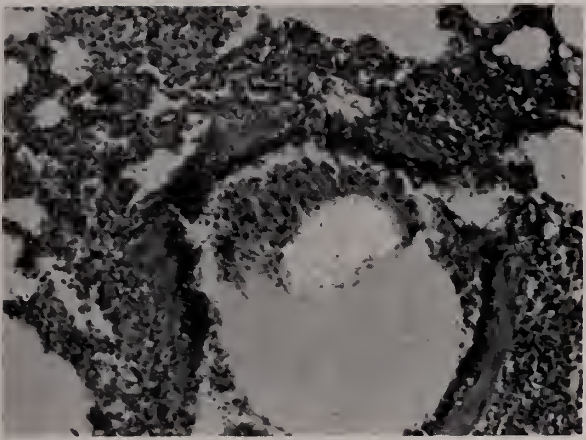

Fig. 3 *(a)* — Appearance of tissue sections under polarized light showing double refractile nature of contrast medium. Resected lobe 48 hours after bronchography. Note doubly refractile material within the bronchial lumen (hematoxylin and eosin; x200).

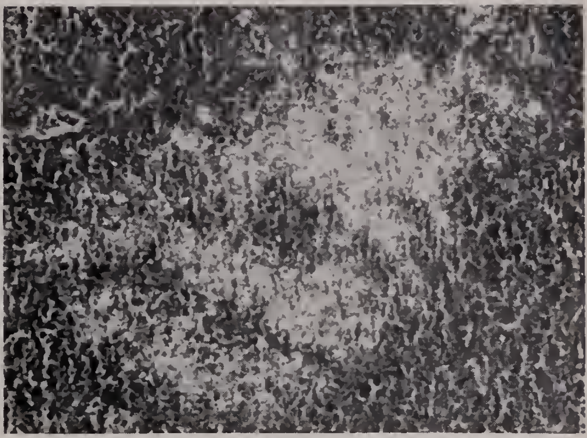

Fig. 3 *(b)* Hilar node removed with the specimen shown in "a." Note deposition of doubly refractile medium (hematoxylin and eosin; x200).

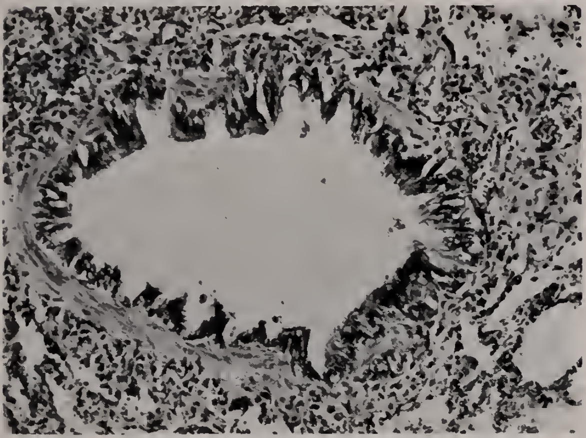

Fig. 4 *(a)* — Section of lung removed 48 hours after bronchography. Note peribronchial response around one of the larger bronchi (hematoxylin and eosin; x200).

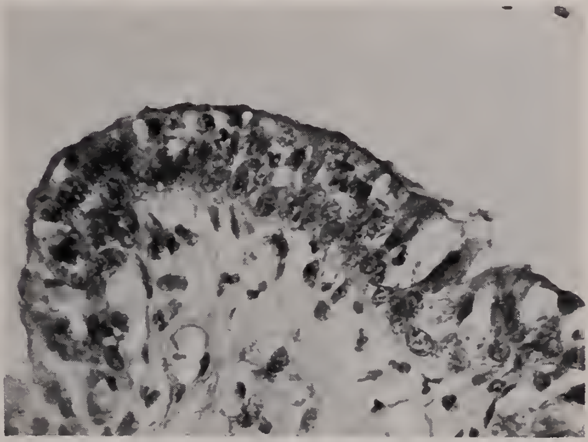

Fig. 4 *(b)* Higher power view of a bronchiole from specimen shown in "a." Note hyperplasia and thickening of mucosa with occasional mitotic figures (hematoxylin and eosin; x600).

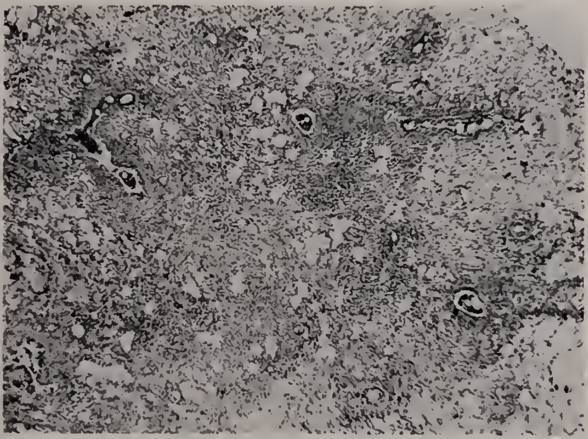

Fig. 5 *(a)* Section of lung removed 48 hours after bronchography. Low power. Note the patchy pneumonitis (hematoxylin and eosin; 25).

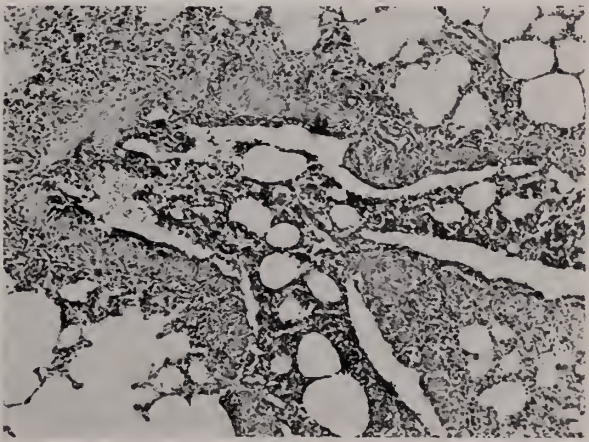

Fig. 5 *(b)* Higher power view from same specimen, showing bifurcation of terminal bronchiole. Note exudate within lumen and peribronchial inflammation (hematoxylin and eosin; x200).

identified microscopically. The microscopic findings consisted of focal areas of interstitial pneumonitis with some thickening of alveolar walls and some peribronchial fibrosis (Fig. 7).

Comment

It is generally recognized that whenever bronchography is performed, a certain optimal period should pass before operation is carried out. The exact length of this period is a subject of considerable controversy. Studies have been made that suggest that the changes in pulmonary function which occur after bronchoscopy disappear after 48 hours when iodized oil is used as the medium, even though there is roentgenologic evidence of retained medium.[2] In patients with advanced pulmonary disease, however, retention of iodized oil may affect gas exchange significantly.[3]

Studies carried out with iodized oil as the contrast medium have shown persistent pathologic changes within the lung parenchyma. Medium could be identified on thoracic roentgenograms months after it had been instilled in the bronchial tree.[4,5] Various water-soluble media have been studied and found to produce a variety of parenchymal lesions.[6,7] These were often manifested, after bronchography, by clinical symptoms such as fever and increased pulse and respiratory rates.[8] Oily propyliodone (Dionosil) seems to produce the least irritative response in the respiratory tract, the effects being similar to those induced by physiologic saline.

The particular medium used in this study provoked a considerable irritative response from the respiratory tract of a dog, the major part of which was seen in the terminal bronchioles and alveolar ducts. The fact that this medium was birefractile made identification of it in the tissues relatively easy. Even the smallest particles could be seen readily. Although it has been reported that the material is not cleared from the lung by way of the lymphatic system, it is interesting to note that, with the polarizing light microscope, medium was seen in the hilar nodes removed

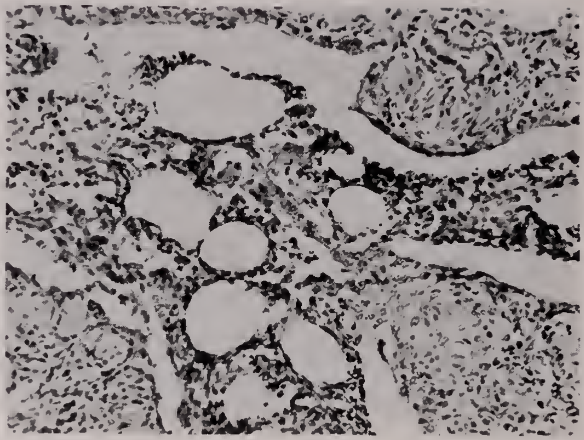

Fig. 5 *(c)* — Higher power view of same area shown in 5 *(b)* showing exudate in the lumen (hematoxylin and eosin; x400).

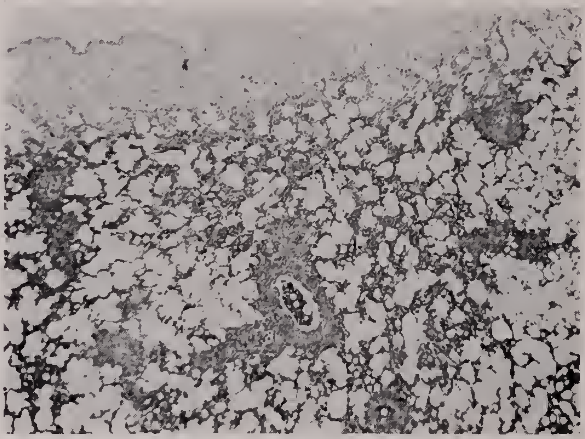

Fig. 6 — Section of lung removed six weeks after bronchography. Inflammatory reaction persists, and there is some peribronchiolar reaction with exudate still present in the lumen of the terminal bronchioles (hematoxylin and eosin; x25).

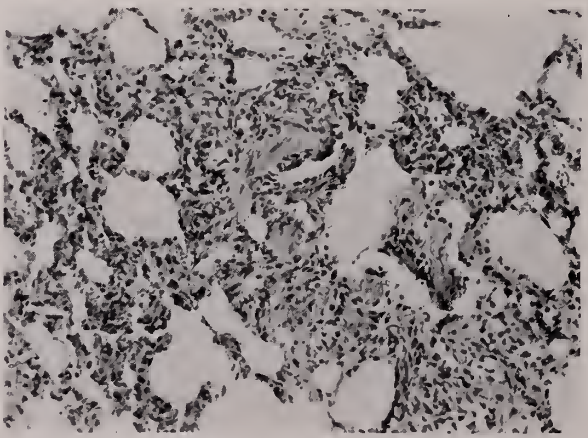

Fig. 7 — Section of lung removed six months after bronchography. Note areas of patchy fibrosis (hematoxylin and eosin; x200).

48 hours after bronchography had been performed.

The histologic findings of parenchymal fibrosis in the dog that was sacrificed six months after bronchography suggest that some permanent damage can occur in the lung exposed to this bronchographic medium, even though this damage may not be detectable clinically.

In the zealous effort that accompanies the trial of various bronchographic media, it should be remembered that the instillation of foreign material into the respiratory tract represents a hazard to the patient, which is measured by the amount of irritative effect of the particular medium. Although the search for a more perfect medium should continue, caution must be exercised that good bronchographic detail is not achieved at the expense of increased risk to the patient.

Summary

Pathologic findings present after instillation of a water-soluble bronchographic medium into the right lung of four dogs reveal histologic findings of parenchymal fibrosis, six months after bronchography. It is suggested that this medium can exert a deleterious effect, even though there was no evidence of retention of it on roentgenographic, gross or microscopic examination of the lung.

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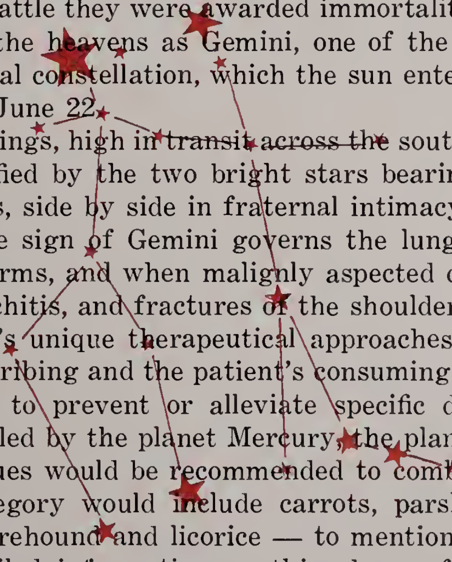
Astrology and Medicine — Gemini, The Twins



In Roman legend Castor and Pollux were brothers, notable for their skills — Castor in managing horses and Pollux in boxing. For distinguished military service in battle they were awarded immortality by Zeus, who had them translated to the heavens as Gemini, one of the three human signs and the third zodiacal constellation, which the sun enters about May 22 to remain until about June 22.

On February evenings, high in transit across the southern sky, the Twins can be easily identified by the two bright stars bearing their names and marking their heads, side by side in fraternal intimacy.

Astrologically, the sign of Gemini governs the lungs and bronchi, also the shoulders and arms, and when malignly aspected disposes to tuberculosis, pleurisy, bronchitis, and fractures of the shoulders, arms, and hands.

One of Astrology's unique therapeutical approaches to disease consists of the doctor's prescribing and the patient's consuming the planetary plant elements calculated to prevent or alleviate specific disorders. Since the sign of Gemini is ruled by the planet Mercury, the plant products endowed with Mercurial virtues would be recommended to combat Gemini morbidities. This food category would include carrots, parsley, caraway seeds, walnuts, filberts, horehound and licorice — to mention only a few.

For further detailed information on this phase of astrological therapeutics, the curious may consult Astrological Keywords by Manly Hall, The Hall Publishing Company, Los Angeles, 1929.

Cyclic Myositis

- *A*
- *Cortisone-*
- *Related*
- *Variety*
- *of*
- *Dermatomyositis-*
- *Polymyositis*

DERMATOMYOSITIS IS a disease in which the involvement of the skin and muscles may last for years and which follows a variable course. The course has been described as acute, chronic, or recurrent. The acute, severe form and the chronic, debilitating form constitute almost all of the cases of this disease observed at the Mayo Clinic (Table 1). A third pattern referring to episodes that occur a year or more apart can be defined as the uncommon, recurrent form. We wish to report the particular qualities of a fourth pattern in myositis which has been observed since the use of corticosteroid therapy and which we call "cyclic myositis" or "cyclic dermatomyositis-polymyositis."

Cyclic myositis is characterized by recurrent exacerbations of myositis that follow clinical and laboratory evidence of remission induced by corticosteroids. The flare does not necessarily follow complete steroid withdrawal. In each instance repeated flares have resulted in steroid administration for years so that the course of clinical findings and steroid dosage is up and down like that of a roller coaster.

Case History

A 3½-year-old white boy with muscle weakness was brought to the Mayo Clinic. His birth and development had been normal. In April, 1956, he had had an episode of fever and coryza, and his parents had noted slowness in his running and walking. In the next two weeks there was regression to inability to climb stairs, raise the arms, or get onto a chair. There was never a complaint of pain or discomfort. The boy had been hospitalized with a diagnosis of Guillain-Barré syndrome. From June to October, 1956, improvement occurred with bed rest; the patient was more active, better co-ordinated, and able to use his arms enough to help with dishes and to handle toys. In the fall of 1956, two episodes of upper respiratory infection were accompanied by increased weakness progressing to almost total incapacity.

Examination in December, 1956, revealed marked weakness of the proximal muscles of the extremities. The boy walked with a waddling gait and was unable to climb onto a sofa or to rise from a recumbent

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TABLE I

Clinical Pattern of Dermatomyositis in 290 Cases

Pattern	Cases
Chronic	232
Acute	42
Recurrent	7
Cyclic	9
Total	290

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position. He could not hold his arms at shoulder level against gravity. The only cutaneous finding was a livid scaling area involving the middle of the forehead and both eyebrows.

Electromyographic examination of the left quadriceps femoris and left biceps brachii revealed fibrillation potentials in the resting muscles. During voluntary contraction, action potentials of the motor units were low in amplitude and consisted of spikes of short duration or polyphasic potentials with spikes of short duration. The proportion of polyphasic potentials was greater than that found in normal muscle. The mean duration of 30 action potentials in the biceps brachii was 3.9 milliseconds, about 60 per cent of the mean value for normal muscle measured by the same technic. The number of potentials relative to the strength of contraction was greater than normal. Conduction velocity of motor fibers of the ulnar, median, and peroneal nerves was normal, although the summated muscle action potentials evoked by stimulation of these nerves were greatly reduced in amplitude. The findings were compatible with myositis.

Biopsy of the left quadriceps muscle revealed that some muscle fibers were in various stages of degeneration and regeneration. These were scattered diffusely throughout the specimen. Increased variation in diameter of muscle fibers and a slight increase in amount of endomysial connective tissue were observed. Two small vessels were surrounded by lymphocytes and plasma cells. The abnormalities were consistent with a diagnosis of myositis. The value of serum transaminase was 535 units per milliliter (upper limit of normal is 86 units). Results of other laboratory studies at this time were normal.

Treatment and Course

Treatment was started with 60 mg. of hydrocortisone a day, and the value of serum glutamic oxalacetic transaminase decreased rapidly to normal. Administration of hydrocortisone was discontinued in July, 1957. At this time the boy had improved markedly; he could climb a ladder, but the quadriceps femoris and biceps brachii muscles were still weak, and he still had a minimal waddle in this gait.

Clinical Improvement Temporary

Monthly examinations showed clinical improvement, but in November, 1957, when the patient's strength was considered improved, serum transaminase was 12.1 μmoles per hour per milliliter (upper limit of normal is 1.43).

In December the mother informed us that the boy's weakness had returned and that he was unable to climb stairs. Treatment with hydrocortisone was started again with 60 mg. per day. Dosage was then changed to 12 mg. of triamcinolone (Aristocort) per day. On neurologic evaluation the muscles of the shoulder and the pelvic girdles were graded as 25 per cent of normal strength. Serum transaminase values decreased to within the normal range during the next five months, and the dosage of steroids was correspondingly decreased. In June, 1958, the patient had Cushing facies, hirsutism, and obesity of the trunk, but his muscle strength was considered normal. By October, 1958, the serum transaminase value had been normal for four months, the myositis was apparently arrested, and administration of steroid was stopped.

Clinical and Laboratory Remission

When the patient returned for a routine examination in January, 1959, he had been attending kindergarten every day. No increased weakness was noted on examination, but he seemed more irritable than usual. At this time his serum glutamic oxalacetic transaminase was 8.52 μmoles. For this reason he was given triamcinolone, 8 mg. per day. The serum transaminase value returned to normal during the next four months, and the hyperirritability disappeared. Muscle strength, which had been decreased in February and March after the administration of steroid was started, improved again with continued therapy. Improvement was concurrent with a decrease of serum glutamic oxalacetic transaminase (Fig.).

In September, 1959, the weight and height of the patient were normal for his age. He had not had any steroids for two months, and the serum transaminase value was slightly elevated to 2.04 μmoles. Two weeks later the transaminase value was 2.83 μmoles. An electromyogram showed improvement from 1956 but still revealed definite abnormalities. The patient was given 10 mg. of hydrocortisone four times a day. In October, 1959, he was improved clinically and was able to return to school. However, the serum transaminase value was 3.48 μmoles, and it continued to rise. Muscle strength appeared to be satisfactory for daily activities, but muscle testing revealed definite weakness in all proximal muscle groups of the extremities. By May, 1960, serum transaminase values were normal and the dosage of hydrocortisone was again decreased. In July, 1960, muscle strength was excellent, and muscle testing revealed good strength; the patient could climb without difficulty. The Cushing habitus had disappeared although residual striae were apparent.

The patient continued to take 20 mg. of hydrocortisone daily through the summer of 1960, but in November marked weakness was noted by the patients. The strength of the muscles of the shoulder and pelvic girdles, the deltoid and biceps brachii, and quadriceps femoris was estimated as 25 per cent of normal. The patient was irritable and was having night sweats. Serum transaminase value was 6.02 μmoles per hour per milliliter. The dose of hydrocortisone was increased to 40 mg. per day.

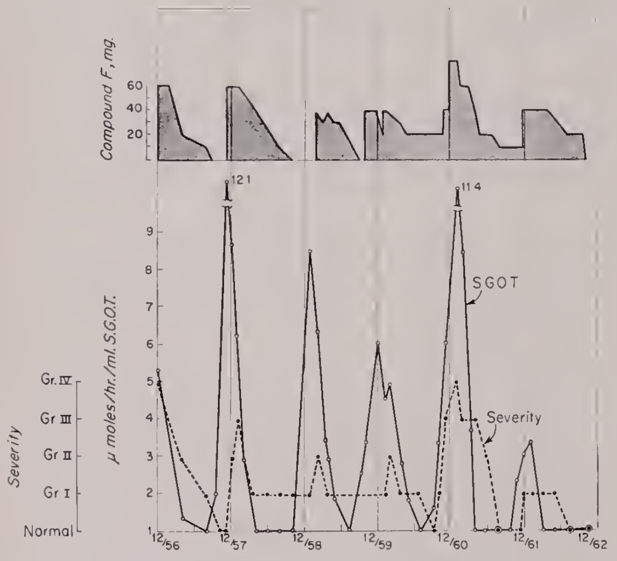

Fig. 1. — A comparison of results of hydrocortisone or triamcinolone treatment with the serum glutamic oxalacetic transaminase (SGOT) values in respect to time. SGOT and clinical course of myositis in relation to variations in dosage (intensity) of therapy with steroids, either hydrocortisone or triamcinolone. Note successive peaks of SGOT values and severity of myositis when steroid therapy was reduced.

Cyclic Pattern

In January, 1961, serum transaminase value was 11.4 μmoles (Fig.), and muscle strength had decreased. The parents stated that a relapse had occurred after rubeola earlier that month. The dose of hydrocortisone was increased to 80 mg. per 24 hours for one week, and serum transaminase values rapidly decreased. The night sweats diminished and irritability disappeared, but generalized muscle weakness could be demonstrated. No dysphagia was present. Therapy was changed to 12 mg. per day of triamcinolone (Aristocort) because of the availability of this drug.

By June, 1961, serum transaminase values were normal, and treatment was 1 mg. of triamcinolone four times a day. In July the patient's strength had improved and was almost normal. For the first time in one and one-half years the patient got up readily from the examining table and was able to climb without difficulty. Serum transaminase value was normal (.97 μmole) in August.

In September, 1961, the patient was receiving the same medication. He had had a cold, and his parents thought that a relapse was beginning because he had been falling oftener than usual. The serum transaminase value was slightly elevated (2.28 μmoles), but since clinical observers stated that the general condition was good, the administration of 1 mg. of triamcinolone twice a day was continued. The value of serum transaminase increased to 12.8 by the end of October, 1961; but the patient's strength at that time was recorded by his consultant as being good. During the next month his mother increased the administration of triamcinolone to 8 mg. per day because she considered his condition worse. Slight Cushing features developed, but by March, 1962, the serum transaminase value was again normal. The boy continued to receive 4 to 8 mg. of triamcinolone daily, and the serum transaminase values remained normal. He was asymptomatic, his strength was improved, and he could walk, climb, and attend school.

In February, 1963, serum transaminase value was slightly increased although muscle strength continued to be satisfactory. The patient was participating in recess activities at school against medical advice. Slight weakness of the muscles of the shoulder and the pelvic girdle was demonstrated on examination. The patient was continuing to take 4 mg. of triamcinolone per day. In July, 1963, electromyographic examination revealed more severe abnormalities than in 1959, but there was no specific evidence of increased muscular incapacity on clinical examination.

The Features of Cyclic Myositis

Nine patients of a study group of 290 patients (Cases 1 to 9, Table 2) with dermatomyositis-polymyositis demonstrated the oscillating course related to steroid therapy illustrated by Case 1. Each of the nine patients has been traced for four years or longer. At time of writing three are in remission after following this cyclic pattern, and six are classified as better although clinically, in most instances, they have continued to have recurrent episodes of muscle weakness accompanied by increased values of serum glutamic oxalacetic transaminase. We have not seen this course in patients who have not received steroids.

Onset of Symptoms

The duration of the illness at the time of diagnosis was less than one year in all cases, and in four it was less than six months. The disease began with cutaneous involvement in three cases, with cutaneous and muscular involvement together in one, and with the principal involvement in the muscles in five.

Of the nine patients, five were female and four were male. The four male patients were children. The age at onset varied from two to 59 years. Eight of the patients were postmenopausal women or prepubertal children, and the ninth was a 16-year-old girl with irregular scanty menses.

Cutaneous changes occurred in all of the patients at some time. Ulceration of the skin occurred in four and was related to calcinosis in two. Such ulcers healed slowly and often were associated with febrile episodes. Contractions were found in three patients. Sensitivity to sunlight was noted in two. Heliotrope-colored eyelids were observed in six, edema of the skin in three, and frank urticaria in one. The chronic, *symmetric erythema of* dermatomyositis was observed in five patients, and this proceeded to the development of poikiloderma in two. *Raynaud's phenomenon* was seen in three patients, two of whom also had sclerosis of the skin compatible with the diagnosis of sclerodermatomyositis.

Fever was a part of the early course in three patients; loss of weight was prominent in only one. *Muscle weakness* was the principal clinical phenomenon, and this weakness progressed until the patients were bedridden in three instances. *Dysphagia* was prominent in four patients, but esophageal roentgenograms showed that peristaltic action was absent in only one patient. Roentgenographic findings were normal in three patients. There was no major joint problem in any, although one patient had had rheumatoid arthritis five years previously.

TABLE 2
Nine Cases of Cyclic Dermatomyositis-Polymyositis

Case	Sex and age at onset, yr.	Duration of treatment, yr.	Number of cycles	Present status
1	M,2	7	5	Continued treatment in 1963
2	M,4	5	4	Remission
3	M,4	4	4	Remission
4	M,9	6	4	Continued treatment in 1963
5	F,16	9	4	Continued treatment in 1961
6	F,41	4	4	Continued treatment in 1960
7	F,46	5	6	Continued treatment in 1963
8	F.48	7	3	Remission in 1963
9	F,59	3	3	Continued treatment in 1963

Transaminase Level

Levels of serum glutamic oxalacetic transaminase were elevated in five patients. Otherwise, laboratory appraisal did not show consistent results. The L. E. cell test was positive in one. Basal metabolic rate was more than +10 per cent in four. The sedimentation rate was more than 10 mm. in one hour (Westergren) in seven of the nine cases, and the highest value was 52 mm. There was no correlation between the severity of the disease estimated clinically and the sedimentation rate. In one patient, the serum albumin-globulin ratio was reversed.

In all nine patients, the initial amounts of steroid that were received were more than 50 mg. per 24 hours.

Comment

Apparently, the cyclic course of myositis with steroid administration develops in a special type of patient. The patients in our series were female with the exception of four prepubertal males. Eight of the nine patients were not in the sexually mature era of life, being either children or postmenopausal women. The only other notation in the literature relating dermatomyositis to sex is that of Muller and associates[1] who found that calcinosis developed in a greater proportion of females than males.

The myositis from which these patients suffered was severe. It had come on rather acutely in all patients and had produced grade 4 muscular incapacity during some stage. Contractures, disability, and calcinosis were frequent in this group despite the administration of steroid. The skin was involved to some extent in all cases, and the entire range of types of cutaneous involvement in dermatomyositis was displayed. Sensitivity to sunlight, erythema, edema, poikiloderma, Raynaud's phenomenon, and sclerosis were all seen in these patients.

One characteristic of cyclic myositis is its prolonged course. All of the patients have had their myopathy a minimum of three years, and the disease continues in the majority of these patients. While the administration of steroid brings symptomatic and objective relief, it does not shorten the course.

Speculation as to why this cyclic form of myositis occurred may begin with the fact that those who developed this course were a special group of prepubertal or postmenopausal female or prepubertal male patients with acute myositis who were early given a high dosage of steroids. None of the patients who had chronic myopathy and who were given steroid therapy demonstrated this course. Steroid suppression of the symptoms of the disease may also suppress the capacity of the body to resist this type of muscle inflammation and degeneration. Although the symptoms are suppressed, the disease remains. Therefore, with withdrawal of the medication, the pathologic process reasserts itself. In Case 1 it was not necssary to discontinue administration of steroids in order for a flare of the process to occur. In fact, the last flares occurred even though a maintenance dose of steroid, which had appeared adequate on previous occasions, was continued.

Complications of Steroid Therapy

Complications of steroid therapy were minimal in our nine patients. Cushing facies, hirsutism, and redistribution of body fat were common, but otherwise no serious complications were encountered although steroid was used for as long as nine years in some of these patients. The dose would be considered high as conservatively defined by Mulder and associates.[2]

Physical activity may affect the course of illness in these patients. In our Case 1, flares occurred in the fall of the year when the patient returned to school and to more active participation in school activities. Many of the patients had annual flares. Flares of the myopathy have occurred in symptomatically well-controlled patients after active participation in work or play or in carrying out strenuous physical therapeutic programs. For several of our patients who had cyclic myopathy, assiduous attention to physical exercise was a feature of the home program. It seems likely that the flares that occurred when the patients were taking only small doses of steroid possibly were induced by excessive physical work of an involved muscle.

Successful treatment of dermatomyositis or polymyositis seems to require the balance of (1) appropriate steroid therapy, (2) nutrition to overcome the negative nitrogen balance that is common, and (3) mild physical exercise that is calculated not to aggravate the disease process in the muscle but that is adequate to maintain a normal physical range of motion and to prevent the development of contractures of muscles and tendons.

Summary

In the nine cases of cyclic dermatomyositis-polymyositis studied, a chronic up-and-down course in dermatomyositis-polymyositis appeared to be related to steroid therapy and has been observed only in patients treated with corticosteroids. Prolonged therapy with steroid may not produce remission of the disease although signs and symptoms are suppressed. In such patients steroid withdrawal is accompanied by a flare of myositis. Because flares of the disease process occur in a cyclic manner, often in relation to physical exercise and despite continuance of maintenance doses of steroid, the appropriate therapy of myositis is thought to depend on the balance of steroid therapy, nutrition, and physical activity.

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Primate — Homo Sapiens

Australopithecus

If you will go to the bathroom, lock the door, and observe yourself closely with neither shame nor pretension, you will discover yourself in the presence of a mammal so primitive and so generalized as to be difficult to describe. You have no distinctive horns arranged like a musical instrument on top of your head. Nobody would dream of shooting you for your tusks. Your hide is worthless, your vestigial fur of comic proportions. No intricate patterns adorn your surface; it has neither the camouflage value to make possible your vanishing into a landscape, nor such decorative value as to warrant your being nailed to a wall. Your teeth lack any special superiority, either for munching hay, chiselling through doors, or penetrating jugular veins. Your claws are so inadequate that while a kitten may scratch you, you cannot scratch the kitten back. And while it is true that you are warm-blooded, and that you do not lay eggs, and that you are edible, still the same may be said of all other mammals. How any creature could survive at least one hundred million years of mammalian evolution and acquire as few specializations as yourself is the chief wonder with which you might attract the attention of a zoologist visiting from another planet. — Robert Ardrey: African Genesis, Atheneum Press, N. Y., 1961.

Violence in the voice is usually the death-rattle of reason. — Arkansas Methodist

WHAT'S YOUR DIAGNOSIS?

A lady, age 72, was admitted October 2, 1964, with a history of five days of intermittent abdominal pain and vomiting, progressing to more steady abdominal pain and profuse vomiting.

There had been intermittent similar episodes of a more mild degree since April 1964. In that month because of these complaints colon and stomach X rays were done and were negative.

The patient had long-standing moderate hypertension, with a more severe elevation occurring in January 1964. Treatment consisted of attempted weight reduction and Esidrix-K, this medication being discontinued in June 1964 and no other medication given. A more remote past history related a cholecystectomy for stones in September 1942; epigastric distress in March 1944, treated with antacids which brought relief, and a gastrointestinal X ray which failed to reveal any ulceration or other abnormalities; curettage in May 1948, which revealed carcinoma of the body of the uterus, followed by a panhysterectomy preceded by X ray therapy; in September 1950, fulguration of an irradiation ulcer within the bladder, followed by healing; in 1958, examination essentially negative in a study of intermittent diarrhea, probably related to prior X ray therapy. That problem subsided without specific therapy.

Physical examination on this admission revealed blood pressure of 160/90, 190/100, 180/108. Pulse 70— regular. Weight 185. Abdominal distention with borborygmi present, no tenderness, distention moderate at 2+; rushes of bowel sounds occurring every two to three minutes with normal sounds in the intervals, and colic associated with peristaltic rushes. Pelvic examination revealed vaginal-wall constriction, no masses.

X ray revealed a moderate amount of small-bowel gas and some in the colon, with small-bowel fluid levels in the upright position.

The findings were suggestive of inhibitory ileus, but partial obstruction of the small bowel could not be ruled out.

Laboratory work: Hemoglobin 14.3; WBC 6,125 with 73% PMN'S; Amylase 23; BUN 11; CO_2 31.4; Chloride 97.5; Sodium 139; K 4.1.

What's Your Diagnosis? Turn to page 180.

ITS THE LAW

Failure to Refer Patient to Specialist Constituted Negligence

In an action by a patient against a doctor for damages for his alleged negligence in setting the four-year-old patient's elbow fracture in a closed reduction, there was evidence from which a jury could find that the doctor was negligent in failing to refer the patient to an orthopedic specialist and that this was the proximate cause of the patient's injury, the Michigan Supreme Court ruled. There was also damage to the epiphysis of the elbow. When the patient continued to have trouble with the arm, an orthopedic surgeon performed several corrective operations. A general practitioner who testified for the patient stated that the doctor violated the standard of practice in the same or similar localities by failing to refer the patient to an orthopedic specialist who, in his opinion, would have discovered the damage to the epiphysis of the elbow at the outset and would have set the fracture by open reduction and the insertion of noncorrosive pins.

The orthopedic specialist who performed the corrective surgery testified that he could see the epiphyseal injury on the original X rays taken by the doctor. This was evidence from which a jury could find that, if the patient had been referred to an orthopedic specialist immediately, his arm would not have been permanently and painfully injured, the court ruled.

Morgan v. Engles, 127 N. W. 2d 382 (Mich., Apr. 6, 1964)

Cirrhosis of the Liver in Pregnancy

*A Case Report and Review of the Literature**

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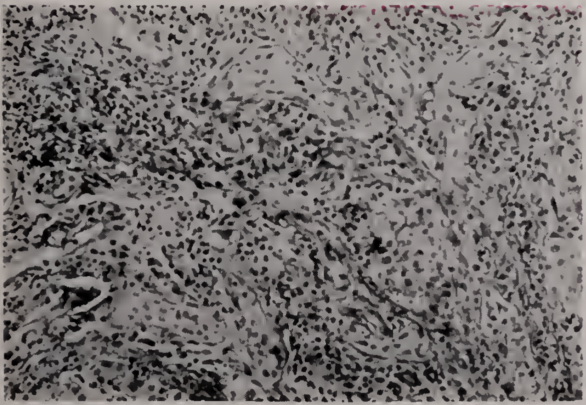

Fig. 1 — Liver biopsy.

THE OCCURRENCE of pregnancy in a patient with cirrhosis of the liver is rare, there being only 35 cases reported. The reason for this infrequent association seems to be the secondary amenorrhea with infertility produced by this debilitating disease.[1] The purpose of this paper is to present the 36th case and to review the literature.

Case Report

A 33-year-old white female was admitted to the University of Minnesota Hospitals on January 30, 1964, for the second time. Her pertinent medical history dates back to 1954 when she had a cholecystectomy performed, which was complicated by a postoperative biliary stricture. An unsuccessful attempt at surgical repair was made at that time. From 1954 to 1956 the patient had recurrent episodes of chills, fever, abdominal pain, and jaundice. Abnormal liver function studies were found which included a total serum bilirubin of 5 mgm.%, cephalin flocculation of four plus, and an alkaline phosphatase of 27 King-Armstrong units. In 1956 a choledochojejunostomy was performed with only partial relief of symptoms. This operation was redone in 1957. The liver at that time was described as being "enlarged, firm and nodular." *A biopsy was performed which showed scarring compatible with the diagnosis of cirrhosis* (Figure 1). From 1957 to 1963 the patient did well, had minimal pain and normal liver function tests. She has never experienced gastrointestinal bleeding.

The patient's obstetrical history included three uncomplicated term deliveries prior to 1954. In 1959 at 30-weeks gestation the patient was referred to the University of Minnesota Hospitals for evaluation. The liver function studies at that time are shown on Table 1. Of note are the reversed A/g ratio, elevated cephalin cholesterol flocculation test, increased thymol turbidity, and an increased brom sulph phthalein retention.

In 1961 the patient had a spontaneous abortion at 20-weeks gestation, cause unknown. The pregnancy did not alter her liver-function studies. At 38-weeks gestation the patient was referred to the University Hospitals on February 14, 1964. Her course had been uncomplicated until three weeks prior to her admission when she developed anasarca and hydramnios, with an associated increase in right upper quadrant abdominal pain and jaundice. The patient's fluid retention was unchanged by treatment with low salt diet, bed rest and thiazide diuretics.

The physical examination showed a jaundiced patient with edema, ascites, and hydramnios. The temperature and blood pressure were normal; the fetal heart tones were normal. The admission laboratory results are shown on Table 1. At that time the laboratory tests showed normal cephalin cholesterol flocculation and thymol turbidity, but there was an elevated bilirubin, brom sulph phthalein retention, and alkaline phosphatase. The total protein concentration was lower with a persistent reversal of the A G ratio.

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*Presented at the Minnesota State Obstetric and Gynecologic Society Meeting, May 9, 1964, at Rochester, Minnesota.

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It was apparent that the fluid retention was due to a decreased plasma colloidal osmotic pressure. The patient was treated with intravenous plasma and salt-free albumin. She also received a one-gram-per-day sodium diet, bed rest, and diuretics. A rapid diuresis was produced. On February 16, she spontaneously began labor, and after a total labor of two hours and 47 minutes she spontaneously delivered a 2600-gram normal female infant which survived. The umbilical cord bilirubin and serum proteins with A/G ratio were normal. The patient's massive diuresis in the first seven hospital days and the removal of the pregnancy decreased her weight by 38 pounds. She was discharged from the hospital on the 12th post-partum day and has done well subsequently. Her liver function was studied nine weeks post partum and is shown on Table 1. Of note are the elevated cephalin cholesterol flocculation test and increased thymol turbidity.

TABLE I

Liver Function Studies

Test	1959	1/30/64	Postpartum
Hbg. (gm. %)	11.5	12.1	11.3
W.B.C. (cell/mm.^{3})	4,700	5,550	6,100
Electrolytes (meq/l)	not done	normal	normal
B.U.N. (mgm. %)	not done	7	11
Serum bilirubin (mgm. %)			
one minute	0.4	2.1	0.4
total	1.0	3.8	0.8
Prothrombin time (seconds)			
patient	13.5	11.7	11.5
control	12.6	11.5	12.0
Cephalin-cholesterol	3+	negative	2+
Thymol turbidity	7	2	8
Total serum proteins (gm. %)	6.7	5.7	7.2
Albumin	2.6	2.0	3.4
Globulin	4.1	3.7	3.8
Alk. phosphatase (K.A. units %)	11.3	26	9
B.S.P. (% retention 45 minutes)	24	28	not done

Discussion

In 1957 Abrams found 15 reported cases of cirrhosis of the liver and pregnancy in the English literature and added two of his own. Since that time 18 additional cases have been reported, bringing the total to 35.

Of the 35 cases, 24 were delivered vaginally. There were five maternal deaths. In no case was the pregnancy considered to decrease the liver reserve. Bleeding from esophageal varices is an important cause of maternal death and both splenorenal and portacaval shunt operations have been done during pregnancy.[12,14,16,17] There is no change in the expected outcome of the liver disease due to pregnancy.

Five fetal deaths have been reported. In two cases the mother died undelivered; a third infant had a congenital abnormality incompatible with survival; a fourth infant died of intracranial hemorrhage; the fifth case was a stillborn of unknown cause. The fetal outcome in one case is not reported. The corrected fetal mortality is not increased.

Many studies have been reported of the normal variations in liver function tests during pregnancy. All of the tests remain normal in the first trimester. At term the brom sulph phthalein, cephalin cholesterol flocculation, thymol turbidity and bilirubin remain normal. There is a progressive elevation of the serum cholesterol and alkaline phosphatase levels during the second and third trimesters, also a decreased serum protein concentration, principally due to an albumin decrease.[19-22]

The present case is interesting in that the liver function tests deteriorated during pregnancy. Since exogenous estrogens can cause an exacerbation of liver disease it has been postulated that pregnancy will do the same.[1] Perhaps this is a case in point. This patient's main problem was fluid retention due to her low plasma protein concentration. The proteins are mainly produced by the liver. Their production capacity was probably limited before pregnancy and with the superimposed "pregnancy-albumin-decrease" a critically low colloidal osmotic pressure developed and fluid retention occurred. This readily responded to exogenous albumin.

The advocated mode of delivery is by the vaginal route unless gastrointestinal bleeding is a problem. With bleeding varices cesarean section is recommended.[16]

Conclusion

Cirrhosis of the liver is an uncommon complication of pregnancy. Generally, the disease does not adversely affect the pregnancy nor does the pregnancy adversely affect the disease. The 36th case is reported and the literature is reviewed.

TABLE 2

Reference	Case No.	Age	Diagnosis	Method of Delivery	Maternal Outcome	Fetal Outcome
Scaglione 1923 (3)	1	25	Autopsy	Spont.	Died 14 hrs.	Unkown
Hesseltine 1930 (4)	2	42	Lap	Spont.	Lived	Lived
Tenny & King 1933 (5)	3	20	Lap	C-section	Lived	Lived
Ashton 1934 (6)	4	25	Autopsy	Spont.	Died 6 mos.	Lived
Lascano & Peyreyra 1936 (3)	5	37	Autopsy	Spont.	Died 19 days	Stbn.
Javert & Morrison 1951 (7)	6	Unknown	Clinical	Spont.	Lived	Lived
Javert & Morrison 1951 (7)	7	Unknown	Clinical	Spont.	Lived	Lived
Javert & Morrison 1951 (7)	8	Unknown	Clinical	Spont.	Lived	Lived
Burslem, Gardikas & Israels 1952 (3)	9	30	Clinical	Spont.	Lived	Lived
Burslem, Gardikas & Israels 1952 (3)	10	24	Biopsy	Spont.	Lived	Lived
Burslem, Gardikas & Israels 1952 (3)	11	25	Biopsy	Spont.	Lived	Lived
Mack 1953 (8)	12	28	Biopsy	C-section	Lived	Lived
Mack 1953 (8)	13	27	Lap	Hyst.	Lived	Lived
Slater 1954 (9)	14	29	Biopsy	Spont.	Died 1 yr.	Lived
Bearn, Kunkel & Slater 1956 (9)	15	27	Biopsy	Forceps	Lived	Lived
Abrams 1956 (2)	16	27	Biopsy	Spont.	Lived	Lived
Abrams 1956 (2)	17	28	Biopsy	Spont.	Lived	Lived
Nabriski 1956 (10)	18	34	Biopsy	C-section	Lived	Lived
Nabriski 1956 (10)	19	27	Biopsy	C-section	Lived	Lived
Nabriski 1956 (10)	20	29	Biopsy	C-section	Lived	Lived
Moore 1959 (11)	21	36	Biopsy	Spont.	Lived	Lived
Moore 1959 (11)	22	29	Biopsy	Forceps	Lived	Lived
Moore 1959 (11)	23	33	Lap	Forceps	Lived	Lived
Moore 1959 (11)	24	35	Lap	Spont.	Lived	Died - Cong. anomalies
Adno 1957 (12)	25	24	Biopsy	C-section	Lived	Lived
Adno 1957 (12)	26	26	Biopsy	Spont.	Lived	Lived
Ohio State Med. J. 1958 (13)	27	40	Biopsy	Undelivered	Died	Died
Fish 1958 (14)	28	17	Lap	C-section	Lived	Lived
Lably 1960 (15)	29	21	Lap	C-section	Lived	Lived
O'Leary & Bepko 1962 (16)	30	33	Lap	Forceps	Lived	Lived
Nelson & Loughead 1963 (17)	31	24	Lap	Forceps	Lived	Lived
Nelson & Loughead 1963 (17)	32	21	Lap	Forceps	Lived	Lived
Slaughter & Krantz 1963 (18)	33	19	Lap	Forceps	Lived	Died
Slaughter & Krantz 1963 (18)	34	21	Lap	C-section	Lived	Lived
Slaughter & Krantz 1963 (18)	35	20	Lap	C-section	Lived	Lived
Shattuck & Spellacy 1964	36	33	Biopsy	Spont.	Lived	Lived

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Pliny's* Cure for Toothache

Pliny recommended the ashes of deer's horns to strengthen loose teeth or allay toothache. This was used either as a friction or as a gargle. He indicated that some people, however, are of the opinion that the horn, unburnt and reduced to powder, is still more efficacious. The hare's rennet is sometimes injected into the ear for this purpose; and the pastern-bone of an ox, ignited and applied to a loose tooth with ashes, has the effect of tightening the teeth in their sockets. When the teeth have been loosened by a blow, they are strengthened by applying asses' milk or else the ashes of the burnt teeth of that animal, or a horse's lichen, reduced to powder and injected into the ear with oil. In referring to the lichen of the horse, Pliny speaks of the excrescence which forms upon the knees of horses just above the hoofs. He mentions that in the heart of the horse there is found a bone** which bears a close resemblance to the eye-tooth of a dog; if the gums are scarified with this bone, or with a tooth taken from the jawbone of a dead horse, corresponding to the place of the affected tooth, the pain will be removed.

Another remedy for diseases of the teeth is joiner's glue, boiled in water and applied, with care being taken to remove it very speedily and instantly to rinse the teeth with wine in which sweet pomegranate rind*** has been boiled. It has also been considered very efficacious to wash the teeth with goats' milk or bull's gall.

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*See Minnesota Medicine June, 1964, Page 716.

**Os cordis in the horse but more prominent in the heart of a cow is found in the aortic ring. In the younger animal it is cartilagenous.

***Pomegranate rind — astringent.

"The American Way"

We live for it, if need be we die for it. We mortgage our future to keep it alive. Some day we hope to agree on what it is. — Senator Soaper

Drugs in Pregnancy*

A warning to all from a world authority: Avoid unnecessary medication during pregnancy.

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THE RECOGNITION in late 1961 of the teratogenic*** effect of thalidomide in man has led to widespread efforts to determine whether other drugs administered during pregnancy may play a contributory role in causing congenital malformations. However, even before the thalidomide episode increasing attention had been directed toward the question of safety of drugs during pregnancy, largely because of the recognition through animal studies and clinical observations that the embryo and the newborn are unable to metabolize many drugs as effectively as the adult. The present paper will review current information concerning the effect on the fetus of drugs administered to the mother during pregnancy and discuss possible means of reducing such drug-induced injury.

Incidence of Malformations

The incidence of congenital malformations has been variously reported as ranging from less than 1 per cent to 8 per cent. Additionally, malformation has been said to occur in some 20 per cent of stillbirths and in a substantial but unknown number of abortions. It is difficult to arrive at a precise estimate of the total number of malformations or the incidence of any given malformation. Observers may vary in their criteria for congenital malformations or in their ability to recognize them. Furthermore, perhaps 50 per cent of congenital malformations are not recognizable at birth. Such factors contribute to the unreliability of data provided from birth certificates. Additionally, eight of the 56 reporting areas for vital statistics do not require the recording of congenital malformations on birth certificates while three do not require a description of the malformation.

Etiology of Malformations

Approximately 10 per cent of human congenital abnormalities are associated with known genetic factors, and a few, perhaps 1 per cent, with known *environmental factors* such as irradiation, German measles, and certain drugs. At present, however, in the vast majority of cases no definite etiology has been established. It is of considerable interest and importance, therefore, to determine what role drugs or other environmental factors may play in producing such deformities, either singly or in combination or conjunction with genetic factors.

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**Chief, Investigational Drug Branch, Division of New Drugs, Bureau of Medicine, Food and Drug Administration, Department of Health, Education and Welfare.

***See Test Your Word Score Page 211.

Effect of Drugs During Early Differentiation

Animal experiments have indicated that a wide variety of drugs may cause congenital malformations or death in the young if given during a critical time during pregnancy. There is little evidence of drug-induced malformations occurring following exposure of the embryo during the predifferentiation period, when the cells still retain their totipotency.* The state of early differentiation appears to be the period of highest susceptibility for congenital malformations. *In man, this extends from about the tenth to about the fiftieth day after conception.* As the various organs and systems become increasingly differentiated, they become less susceptible to teratogenic agents. In all periods, however, the adverse effects of the drug may lead to death of the embryo.

X-irradiation

The first environmental factor to be linked with the production of congenital defects in human beings was x-irradiation. Murphy, in 1928, reported that microcephaly and mental retardation occurred with a high degree of frequency in the offspring of mothers who received x-irradiation to the pelvis during pregnancy. Similar malformations were described in offspring born to mothers who during their early pregnancy were exposed to the atomic bomb exploded in Hiroshima in 1945.

German Measles

In 1941, Gregg in Australia first recognized that German measles in the first trimester of pregnancy was frequently associated with severe congenital malformations in the offspring. The defects most commonly noted are malformations of the heart and of the eye, and microcephaly.

Aminopterin

The teratogenic effect of the folic acid antagonist, aminopterin, was first recognized in 1952 when this agent was used as a therapeutic abortifacient. In 24 pregnant women receiving the drug, four cases of congenital malformations were noted in the eight cases that required surgical intervention because spontaneous abortion did not occur. Defects included central nervous system damage and cleft palate.

Alkylating Agents

Congenital malformations have been reported in children born to mothers with Hodgkin's disease, who were treated with the alkylating agents cyclophosphamide and chlorambucil, respectively, during pregnancy, and in a child whose mother received a combination of busulfan and mercaptopurine during pregnancy for the treatment of chronic myelogenous leukemia. Fetal abnormalities have been produced in animals with a variety of antineoplastic agents administered during pregnancy.

Progestational Substances

The teratogenic effect of certain progestational substances and other steroids advocated for the control of bleeding in pregnancy, or for the treatment of threatened abortion, was first described in 1958. Such drugs given during the first trimester of pregnancy led in a small per cent of cases to masculinization of the external genitalia in the female fetus. Evidence available at this time suggests that the defect carries no functional disabilities, but the condition must be differentiated from the more serious but anatomically similar virilizing adrenal hyperplasia. Finally, the potent teratogenic effect of thalidomide was first reported in late 1961 almost simultaneously by McLeod in Australia and Lenz in Germany.

Thalidomide

The characteristic malformations were limb defects varying from the shortening of a single bone to complete absence of all the long bones of the extremities. Most frequently affected were the upper limbs. Other deformities included absence or deformity of the external ear, absence of the internal ear with deafness, a characteristic birthmark over the forehead and, less frequently, congenital heart disease and intestinal stenosis. Dr. McBride reported that in a series of 40 women receiving thalidomide during the first trimester of pregnancy, 14 (or 35 per cent) delivered babies with deformities now known to be characteristic of thalidomide ingestion.

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*See Test Your Word Score Page 211.

Oral Hypoglycemic Agents

In addition to those drugs which have been clearly implicated in fetal malformations, a number of preparations have been suspected of being teratogens either on the basis of animal studies or on the grounds of somewhat limited clinical observations. For example, tolbutamide has produced congenital malformations in certain animal species, while in one clinical study the use of chlorpropamide was associated with a high perinatal mortality and one case of microcephaly.

While diabetes mellitus itself may predispose to fetal malformations, nevertheless, these findings have led to a questioning of the safety of these oral hypoglycemic agencies in pregnancy. Additionally, clinical experience indicates that, generally speaking, pregnant diabetics are better controlled with insulin than with oral hypoglycemic agents.

Antihistamine Preparations

Two antihistamine preparations, meclizine and cyclizine, have been shown to be teratogenic in some species of animals; and certain clinical studies, but not all, have suggested that such drugs may occasionally have a teratogenic effect in human beings. Again, evidence is hard to establish because of the widespread use of such agents to control nausea and vomiting of early pregnancy and the fact that there may be a somewhat higher incidence of malformations in patients who suffer from the nausea and vomiting of pregnancy. The evidence, however, does suggest that alternate measures of controlling nausea and vomiting should be considered.

The Developmental Stage of Embryo

Although only a few agents have been definitely associated with congenital defects in humans, nevertheless, certain principles established in animal studies appear to apply also to drug-induced teratogenesis in human subjects. In the first place the susceptibility of the embryo depends on the developmental stage at which the agent is applied, as does to some extent the nature and extent of the defect produced. Furthermore, whereas there may be a certain degree of overlapping in the effects evoked by the various teratogenic agents, each agent appears to elicit characteristic effects. Again, the experience with aminopterin illustrates that a drug capable of causing death to the fetus may also lead to congenital malformations under certain circumstances. Finally, the experience with thalidomide demonstrates that a drug can produce profound effects in the embryo without affecting the well-being of the mother.

Ineffective Placental Barrier

Until comparatively recently, it was assumed that the placenta formed an effective barrier to protect the fetus from the passage of drugs and other agents from the maternal circulation to the fetal circulation. It is now recognized, however, that the transfer of substances across the placental barrier is governed primarily by the same physical and chemical laws that determine the transfer of substances across all cell walls.

Effect of Low Lipoid Solubility of the Drug

The chemical nature of cell walls is such that nonionized drugs with high fat solubility are transferred rapidly, while drugs with high degrees of dissociation or of low lipoid solubility either cannot be transferred or are transferred in small amounts only. Additionally, very large molecules or substances bound to plasma proteins may fail to pass the barrier. Similar principles apply to the handling of drugs by the gastrointestinal tract, the passage of drugs through the so-called "blood-brain" barrier, and the localization of drugs in certain tissues or organs.

Pathologic Changes in Placenta

Once the drug has passed the placenta its effect on the fetus will depend on a number of factors, such as the ability of the fetal tissues to metabolize or detoxify the compound, the disposition of the drug or its metabolites in the tissue of the fetus, and the susceptibility of the fetal tissue to the adverse effects of the drug. Additionally, the permeability of the placenta may well be altered by such factors as pathological changes in the placenta, changes in maternal and fetal blood flow of the placenta, and maternal infection, dehydration or hemorrhage.

Metabolic Processes in the Mother

It should be borne in mind that the effect of drugs on the fetus need not necessarily be a direct one. Animal experiments indicate certain drugs may affect the fetus indirectly by interfering with metabolic processes in the mother.

Hyperthyroidism

Drugs that freely pass the placental barrier may elicit pharmacologic and toxic effects on the fetus or newborn similar to those observed during therapy with the drug. Thus, thiouracil derivatives or iodides given to the mother during pregnancy for the treatment of hyperthyroidism or iodides given for asthma may lead to congenital goiter, which may be accompanied by a hyperthyroid, hypothyroid or euthyroid state. Such goiters usually regress spontaneously after delivery when the influence of the drug is no longer present. However, they may be sufficiently large to interfere with normal delivery or to offer mechanical respiratory obstruction after birth, which may require surgical intervention.

Anticoagulants

Anticoagulants administered for the treatment of thrombophlebitis during pregnancy may result in fetal or neonatal hemorrhage and death.

Babies born to *morphine addicts* may have pin-point pupils at birth and may suffer from severe and even fatal withdrawal symptoms; while babies born to mothers receiving *reserpine* may have a characteristic syndrome of stuffy nose and respiratory distress. Large doses of *quinine during pregnancy* have been reported to result in fetal deafness, and 8th nerve toxicity has also been reported for streptomycin.

Growth Retardation in Bone and Teeth

A recently observed adverse reaction to a drug given during pregnancy is that of the staining of deciduous teeth in children whose mothers received a *tetracycline* drug during the last trimester of pregnancy. A similar effect is seen in the deciduous teeth of infants receiving the drug or in the permanent teeth of children receiving the drug from the third up to the sixth or seventh year of life. Apparently tetracyclines have a predilection for bones and the developing tooth. Animal studies indicate they are deposited in the growing bone and may result in some growth retardation that is reversible after discontinuation of the drug. A similar effect has been noted in premature infants.

Fetal Tissues Lack Detoxifying Enzymes

In recent years, it has become apparent that the fetus and newborn may react in a unique fashion to certain drugs. In many instances, this is because the fetal tissues lack many of the enzymes necessary for the detoxification of certain drugs. Additionally, the immature kidney is unable to excrete drugs as rapidly or effectively as the adult.

The "Grey Syndrome"

Sutherland reported that the susceptibility of newborn infants, particularly premature infants, to chloramphenicol was due to the inability of the liver to form the less toxic glucuronide. The resultant high blood level of chloramphenicol leads to cardiovascular collapse, the so-called "grey syndrome." Again, the administration of certain drugs, such as long-acting sulfonamides, novobiocin, and water-soluble Vitamin K may affect the metabolism of bilirubin and lead to hyperbilirubinemia with an increased risk of kernicterus and death. A number of factors appear to be involved. Thus, drugs may compete with bilirubin for the inadequate hepatic enzymes that ordinarily conjugate bilirubin to the less toxic glucuronide.

Destruction of Hemoglobin

The red blood cell of the fetus and the newborn has an enzyme deficiency which predisposes it to hemolysis by various drugs including water-soluble Vitamin K preparations. The increased bilirubin from the destruction of hemoglobin will tax further the inadequate detoxification mechanisms of the immature liver. Additionally, drugs may compete with bilirubin for binding sites on plasma albumin, leading to an increase in free (or toxic) bilirubin.

The recognition of the role of water-soluble Vitamin K preparations in jaundice of the newborn has led to recommendations that when these substances are given to the premature infant in hemolytic disease of the newborn, the maximal daily dose should not exceed 1 milligram. Furthermore, since the safety and effectiveness of administering these preparations to mothers in pregnancy for the prevention of hemorrhagic disease of the newborn has not been established, it is recommended that these preparations be given to the infant after birth rather than prenatally through the mother.

Discussion

It is recognized that tests may well fail to be of any predictive value in regard to the behavior of a drug in pregnancy in human subjects. Many widely used drugs may exhibit effects in one or more species of animals if taken during pregnancy but have not been established as causing adverse effects in man. Alternately, thalidomide fails to exert the same striking teratogenic effect in certain animal species that it does in man and certain other species of animals. However, data on the effect of most drugs on pregnancy in either animals or man are admittedly quite fragmentary. As more data are accumulated, more appropriate screening procedures may be devised.

The procedure presently recommended by the FDA consists essentially of feeding subtoxic doses of the drug under test to male and female rats, for a preliminary period of six weeks and then through two pregnancies. It should be emphasized that this test is intended not only to detect drugs that may cause teratogenic effects but also those which may effect spermatogenesis or fertilization or implantation, or otherwise adversely affect the rat fetus or welfare of the newborn.

Thalidomide tested by this procedure produces few if any fetal abnormalities but causes a significant reduction in litter size. Tested in certain strains of rabbits, another species commonly employed in teratologic screening procedures, it causes fetal malformations not unlike those produced in human subjects.

If preliminary screening tests indicate an adverse effect on the fetus, further animal species should be studied and more information made available concerning such factors as absorption, metabolism, and excretion of the drug in animals and in man. The question as to whether a drug which shows an adverse effect in animal species during pregnancy should be tested in women of the childbearing age may be a difficult one to resolve. In cases of drugs used in life-threatening conditions the use of such drugs in pregnancy may well be justifiable. It is doubtful, however, whether similar risks should be taken for a drug such as a mild sedative or a hypnotic for which there are other preparations available.

Failure to elicit teratogenic effects in animals offers no assurance that the drug can be safely used during human pregnancy. In all cases where new drugs are used in pregnant women, very accurate records should be taken of the time of administration, the amount of drugs given and the duration of therapy. Furthermore, the child should be carefully examined at birth and carefully followed at least through the first year of life.

The report by McLeod indicates that a well-controlled prospective study could readily have demonstrated the adverse effects of thalidomide before it caused such widespread damage, since it produced a high incidence of malformations of a conspicuous nature.

Additionally, if drugs are to be used in infants, it should be required that the LD_{50} be determined in the day-old rat, with the hope that it may be possible to detect any abnormal pattern of detoxification in the newborn. Data submitted indicate that the acute toxicity of certain drugs may vary widely if tested in the newborn and the adult animal. Again, recommendations for pediatric use of a drug must be substantiated by adequate clinical studies to establish the safety and effectiveness of the drug in the appropriate age group or groups.

Conclusion

It is recognized that the growing awareness of the adverse effects of certain drugs on the fetus and newborn presents many practical problems to the physician. With more careful clinical studies and further basic research more definite guidelines may be available for the safe use of drugs during pregnancy.

Unnecessary medication during pregnancy is certainly to be avoided, and in particular women of the childbearing age should be counselled against self-medication.

It must be recognized, however, that some conditions in the mother, if left untreated, may well predispose to adverse effects in the offspring, while others may be so threatening to the life of the mother that it would be unjustifiable to withhold an effective drug for fear of possible teratogenesis.

ANSWER TO WHAT'S YOUR DIAGNOSIS

(From page 170)

The patient was operated on within the first 24 hours after admission. Findings revealed two small narrow areas of constriction in the terminal ileum approximately 24 inches from the ileocecal valve. The area of most marked constriction was 6" distal to one of lesser constriction. All of the remainder of the bowel was of normal color and texture. There were no adhesions by or proximal to the constriction. Slight to moderate distention. Pelvis free of tumor. Periaortic area all normal.

A resection of the involved area and primary anastomosis was accomplished. The patient recovered and was discharged the ninth postoperative day, having an uneventful convalescence.

Pathology: Submucosal fibrosis, marked in 1 cm. area with 3 mm. ulcer on one side of the mucosa, considered to have been caused by enteric-coated Esidrix K which was discontinued in June 1964 because of abdominal distress.

Not only is nature useless, it may even be harmful. A natural healing power, curing diseases by design, is a delusion. The physician must actively interfere with nature. It is the physician's duty to cure safely, quickly, pleasantly: tuto, cito et jacunde.
— *Asclepiades B. C. 100*

Cowardice asks, "Is it safe?" Expedience asks, "Is is politic?" Vanity asks, "Is it popular?" But Conscience asks "Is it right?" — Papyrus

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Difficulty is the excuse history never accepts. — Samuel Grafton

Hemobilia Due to Common Duct. Hepatic Artery Communication Following Operations on the Biliary Tract*

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HEMOBILIA, a term coined by Sandblom of Sweden, designates hemorrhage via the common duct into the duodenum.[14] The most common cause is trauma resulting in a capsular or subcapsular hepatic tear, as originally described by Owen.[12,15] Massive and recurrent hemobilia may also be associated with penetrating hepatic injuries and such conditions as ruptures of hepatic artery aneurysms into the common duct and hemorrhagic cholecystitis.[4,6,10] Bleeding due to ductal wall erosion by a T-tube or a stone was described previously.[13]

The occurrence of hemobilia following common-duct surgery is a rare cause of massive upper gastrointestinal hemorrhage; only occasional reports are listed in the world literature.[2,7] As iatrogenic complications, such cases are not readily reported by the operating surgeon. Several extensive reviews on complications of cholecystectomy do not mention hemobilia.[1,5,11] Kehr referred to erosion of the portal vein and hepatic artery by a common-duct stone.[8] Even though the causes of hemobilia were carefully classified by Kerr and Lichtman, massive hemobilia as an iatrogenic sequela of surgery on the biliary tract was not listed.[9,10] Furthermore, hemobilia was not observed as a complication of biliary surgery in patients operated on at the University of Minnesota Hospitals.

Patients with hemobilia secondary to biliary tract surgery present symptoms similar to those discussed by Sandblom.[14] The inciting trauma differs from cases due to liver injury and may be paraphrased by the referring physician as "difficulty of identifying portal structures associated with bleeding." Pain simulating biliary colic may be followed by gastrointestinal hemorrhage; jaundice may be due to obstructing clots in the common duct or concomitant operative injury to

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the common duct. Accurate preoperative diagnosis is a common problem, and an operative solution may be challenging to both the patient and the surgeon.

In all three patients in this report a cholecystectomy and a common-duct procedure were performed prior to admission to the University of Minnesota Hospitals. In one patient, in addition to a cholecystectomy, the first operation consisted of a Billroth II type gastrectomy for gastric ulcer. In the other patients recurrent episodes of upper gastrointestinal hemorrhage were observed, but no other gastrointestinal pathology was demonstrated with barium contrast. The cause of bleeding was established with certainty only at time of surgery. In one case gastrointestinal hemorrhage was accompanied by bleeding from the T-tube tract.

Despite the difficulties encountered in dissection of the portal area, anatomical relationships could be established in all three patients. Hemorrhage was arrested by ligature of the offending vessel or reconstruction of the bleeding artery, and a successful outcome obtained in two patients. In the third patient the outcome was predetermined by poor liver function due to biliary cirrhosis secondary to a concomitant development of postoperative biliary-duct stricture. An attempt at reconstruction of the hepatic artery with a patch of Teflon and choledoduodenostomy terminated fatally, due to disruption of both repairs. Exsanguinating hemorrhage and bile peritonitis were the terminal events.

Case Reports

Case No. 1

This 56-year-old white female had suffered for some years with right upper quadrant pain diagnosed as chronic cholecystitis and cholelithiasis. On 8/26/63 the patient underwent a cholecystectomy in an outside hospital, at which time the common duct was inadvertently severed and the structure repaired by direct end-to-end anastomosis over a T-tube. On 9/5/63 an episode of bleeding was noted via the T-tube, which became obstructed with clots. The patient received vitamin K and five units of whole blood. Approximately one week later more bleeding was noted around the T-tube. A T-tube cholangiogram was normal. Dark, bloody, liquid stools were noted, and the patient received five more units of whole blood as replacement. An upper gastrointestinal series was within normal limits, with suggestion of questionable compression of the first part of the duodenum. After an essentially asymptomatic interval of three weeks the patient was readmitted to the hospital because of hematemesis and tarry stools, requiring 12 units of blood for replacement. On 10/15/63 she again had to be transfused with 3½ units of blood for gastrointestinal bleeding. On 10/21/63 she complained of epigastric fullness and showed further evidence of upper gastrointestinal hemorrhage. At this stage of her illness she was transferred to the University of Minnesota Hospitals.

The past history of this patient was not contributory, with the exception of dysuria caused by interstitial cystitis and a bladder diverticulum.

Physical examination at the time of admission revealed a temperature of 101.6°, pulse of 104/min., and blood pressure and respiration within normal limits. A large incisional hernia was observed in the place of a previous right pararectal incision, but no tenderness or guarding was noted. Rectal examination revealed tarry stools. A preoperative diagnostic impression of hemobilia caused by communication between the hepatic artery and the common duct was suggested by the initial episode of bleeding from the T-tube. An upper gastrointestinal series was within normal limits and an esophagogram revealed no varices.

The white cell count was within normal limits. The liver function tests were not abnormal during the patient's illness, with the exception of an elevated direct reacting bilirubin (2.85 mg. %) and alkaline phosphatase (20 K. A. units) on one occasion. An intravenous cholangiogram showed visualization of the distal and proximal extrahepatic duct system, but the central portion was hazy. A hepatic artery angiogram was contemplated; the patient, however, developed another episode of acute gastrointestinal hemorrhage. The vital signs stabilized after 1500 ml. of blood was transfused, and an emergency exploratory laparotomy was performed.

Operation

Multiple adhesions containing the small and large bowel were found in the right upper quadrant, and the duodenum was adherent to the area of the common duct. Upon dissection of the posterior wall of the descending duodenum, a 1-cm. pseudo-aneurysmal clot was found interposed between a 3 mm. vessel entering the liver hilus and the right lateral aspect of the common duct. The artery took origin from the gastroduodenal artery. A cavitary area of granulation tissue surrounded this portion of the common duct. Upon further dissection the common hepatic artery was identified to the left of the hepatic duct, and lastly, the right and left branches were demonstrated. It became evident that the cause of bleeding was a communication between an accessory right hepatic artery and the common bile duct with an interposed pseudo-aneurysm of excavated clot. The accessory hepatic artery was ligated and a choledoduodenostomy was performed. The operative procedure, due to multiple adhesions, was complicated by blood loss which could be adequately replaced.

The postoperative course of this patient was uneventful and no further bleeding episodes have occurred. A postoperative cholangiogram revealed a normal duct communication with the duodenum. Upon discharge from the hospital, the patient developed multiple episodes of vomiting, due to partial duodenal obstruction distal to the area of the common-duct anastomosis, explained on the basis of a duodenal ileus. As conservative measures did not improve this situation, a gastroenterostomy was performed. This relieved all symptoms; the patient has remained in good health.

Comment

As a result of an accidental transection of the common duct and possibly some leakage of bile along the T-tube, erosion of an accessory hepatic artery occurred. Two etiological factors must be considered: one possible cause was direct trauma to the accessory hepatic artery at time of cholecystectomy and common-duct surgery; the other factor could have been erosion of the vessel by bile and infection. The recurrence of bleeding was explained by the valve-like mechanism of the above-described pseudoaneurysm or recurrent clot lysis by bacterial enzymes and bile.

Case No. 2

This 34-year-old white female gave a history of jaundice in 1953 associated with right upper quadrant pain. In August 1954, the jaundice recurred, and three weeks later she was operated on in an outside hospital, at which time a cholecystectomy and common-duct exploration were performed. A T-tube placed in the common duct at time of operation was removed in January 1955. Postoperatively, her jaundice had subsided, only to recur with increasing intensity, and associated with hematemesis and melena. In July 1955, the patient started passing tarry or bright red stools in large quantities.

On physical examination this emaciated patient had a firm abdomen due to liver enlargement of four finger breadths below the right costal margin. An upper gastrointestinal series revealed an inactive duodenal ulcer. After multiple transfusions a hemoglobin of 10 gm. associated with recurrent hemorrhage was brought to normal levels. The direct serum bilirubin was 12.2 mg. %, total was 20.7 mg. %, and the alkaline phosphatase was 25.8 K. A. units. The prothrombin time was within normal limits, the BSP showed 13 per cent retention, and the total serum protein was 7.9 gm. % with a reversed A-G ratio of 2.9 and 5.0 gm. %. In view of clear evidence of obstructive jaundice, a preoperative diagnosis of common-duct obstruction due to stone or stricture was made.

Operation

At the time of surgery there were dense adhesions in the right upper quadrant binding the surrounding structures to the porta hepatis. Upon further dissection an old hematoma was noted, and when this was cleared, a sudden gush of blood was seen to originate from the hepatic artery. In an attempt to preserve this essential vessel the artery was repaired, using a pledget of Ivalon. The stricture of the common duct was repaired by choledododuodenostomy. This was accomplished with some difficulty as the proximal end of the common duct was scarred, and only high in the hilus of the liver could a remnant of the common hepatic duct be identified. The postoperative course was stormy, as the patient developed a collection of intraperitoneal bile-stained fluid which had to be drained. In the remaining week of her life she passed large amounts of blood per rectum and also showed evidence of intraperitoneal bleeding, requiring multiple blood transfusions.

The autopsy findings showed massive hemoperitoneum secondary to rupture of the hepatic artery at the site of the repair, biliary cirrhosis secondary to common bile-duct stricture, intrahepatic abscesses, a lysis of the common duct-duodenal anastomosis, and a duodenal ulcer of no clinical importance.

Comment

This patient's history demonstrates the grim aftermath of unfortunate biliary-tract surgery, characterized by common-duct stricture and recurrent episodes of ascending cholangitis. Despite the fact that her condition continued to deteriorate, it was felt advisable to operate, as this appeared to be the only possible avenue of success. The findings of a hematoma suggested past episodes of intraperitoneal hemorrhage.

Only an occasional patient will tolerate ligation of the hepatic artery. Reconstruction of this artery was therefore attempted. Exsanguination from the area of arterial repair clearly indicated that such repairs performed in an infected field are not advisable.

Case No. 3

In September 1958, this patient was admitted to the University of Minnesota Hospitals with a two-year history of epigastric pain relieved by food. A diagnosis of ulceration in the duodenal bulb and a lesser curvature gastric ulcer were established. The patient improved on conservative management; but three months later when massive bleeding occurred from the gastrointestinal tract, an 80-per cent resection of the stomach and a Billroth II reconstruction were performed in another hospital. A cholecystectomy, exploration of the common duct, and insertion of a T-tube were also done. Two weeks after the procedure the T-tube was removed, and the patient was discharged, apparently recovered. One month after this operation the patient was re-admitted with another episode of massive hematemesis and liquid bloody stools, requiring transfusion of 12 pints of blood. The patient was then transferred to the University of Minnesota Hospitals.

At the time of admission the physical examination revealed an old midline abdominal incision; the liver edge was palpated some 4 cm. below the right costal margin. The significant laboratory findings were a BSP retention of 33 per cent, alkaline phosphatase of 12 K. A. units, and serum bilirubin of 2.9 mg. % direct and 5.5 mg. % total. During the first three days of hospitalization the patient had several episodes of upper gastrointestinal hemorrhage requiring replacement with fourteen units of blood. Gastric cooling was instituted with cessation of the bleeding and an operative exploration followed.

Operation

The transverse colon was adherent to the liver. The subhepatic area was found to be filled with a massive blood clot and fresh blood. Upon further identification of portal structures, a large pulsating bleeding vessel was identified as the hepatic artery. A defect with sharp edges was visualized while the bleeding was controlled with compression of the artery through the Foramen of Winslow. An old suture was found in the vicinity of the hepatic arterial tear. This vessel was repaired with running 5-0 arterial silk. The common duct was repaired with interrupted 5-0 chromic catgut sutures, and a Robinson catheter was introduced into the common bile duct for decompression of the biliary tree. With the exception of a minor wound infection, the postoperative course was uneventful.

Comment

This patient suffered both intraperitoneal bleeding as well as hemobilia secondary to an operation on the common duct. The most likely cause was a direct injury to the hepatic artery or traumatization at time of removal of the T-tube.

Discussion

In all three patients bleeding originated from a hepatic artery which communicated with the adjacent common duct, thus producing upper gastrointestinal hemorrhage. In two patients the findings at time of laparotomy showed an abscess-like cavity; in the third patient an opening was observed both in the hepatic artery and in the common duct. The association of hepatic artery common-duct communication with common-duct stricture supports the view that this malady is iatrogenic in origin.

The long history of biliary stricture in the second patient produced cirrhosis and irreversible hepatic changes. In the first and the third cases the relatively short period since the original operation did not allow irreversible hepatic changes to develop and thus treatment by surgical reconstruction could be successfully accomplished. In all three patients the upper gastrointestinal bleeding episodes followed by asymptomatic intervals were similar to the characteristic bleeding found in hemobilia due to hepatic trauma. Jaundice may be caused by absorption of blood from the peritoneal cavity or of bile originating from a common-duct leak and may also be the result of obstruction of the biliary tract. In the second patient bile stasis was undoubtedly due to a biliary stricture; in the other two patients the transient elevation of bilirubin was probably caused by common-duct obstruction produced by blood clots.

Hemobilia must be considered in the differential diagnosis of obscure upper gastrointestinal hemorrhage subsequent to operations on the external biliary system and as an associated finding of common-duct stricture. Presence of a duodenal ulcer identified with a barium contrast examination certainly does not exclude bleeding via the common duct. This type of hemorrhage is difficult to differentiate from other causes of bleeding from the esophagus, stomach, or duodenum. In only one patient was the probable cause suggested prior to surgery. Bleeding around and through a T-tube following common bile-duct surgery should point to this diagnosis. Hemobilia resulting from a communication between the hepatic artery and common duct cannot be excluded by intravenous or T-tube cholangiography. The diagnostic value of identifying a hepatic artery common-duct communication with arteriography requires further evaluation.

Whether reconstruction of an essential vessel such as the hepatic artery can be accomplished must be resolved in each case independently at time of operation. In an infected field such as an abscess cavity, ligation and transfixion of a vessel must be resorted to. The finding in all three patients of an abscess-like cavity containing a mixture of bile with blood in the area of hepatic artery and common-duct communication incriminates bile leakage and direct trauma to the hepatic artery as a causative factor of this entity.

Clearly, the operating surgeon must assume responsibility for this type of hemobilia following operations on the external bile duct system. Prevention must be sought in meticulous dissection and technically proper handling of all the structures while operating on the gallbladder or the common duct.

Summary

Three patient histories of hemobilia secondary to surgical intervention on the biliary tree have been reported. This pathological entity was contrasted with hemobilia due to liver injury. Massive intraperitoneal hemorrhage associated with upper gastrointestinal hemorrhage was present in two patients. Hemobilia should be suspected in all patients with upper gastrointestinal hemorrhage occurring after operations on the biliary tree.

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The Penalty of Overweight

Extensive studies have revealed that elevated blood pressure occurs in obese patients in every age group, and in both sexes. With each increase in body weight there is a steady progression of both the systolic and the diastolic blood pressure. — Cyril M. MacBryde, M.D., Signs & Symptoms, Lippincott Co.

Truth in medicine is a goal which cannot be absolutely reached, and the art of healing, as it is described in books, is far beneath the practical experience of a skillful, thoughtful physician. — Rhazes (865-925)

Pseudo-Pseudohypoparathyroidism

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IN 1942, ALBRIGHT and associates[1] described three patients, each of whom had rounded facial configuration, short thick-set stature, and short fingers. These three patients also showed clinical signs of tetany, low concentration of calcium, and high concentration of phosphorus in the serum. Resistance to parathyroid hormone as measured by the Ellsworth-Howard test was demonstrated. This clinico-phenotypic syndrome was termed "pseudo-hypoparathyroidism." In 1952, Albright and associates[2] described a thick-set round-faced woman with short fingers and toes who had never manifested any signs of tetany and who had normal serum calcium and phosphorus values. Because of the phenotypic resemblance to pseudohypoparathyroidism and because the parathyroid function appeared adequate, they called this syndrome of anomalies "pseudo - pseudohypoparathyroidism." The purpose of our study was to investigate certain aspects of the calcium and phosphorus metabolism in a patient with pseudo-pseudohypoparathyroidism and to attempt to correlate the findings with the results of prior studies.

Our patient was a 47-year-old man who was short and round faced and who had shortening of the metatarsal and metacarpal bones and normal concentrations of serum calcium and phosphorus. The phenotypic characteristics and preliminary laboratory findings on this patient and his sister have been recorded in a prior study.[3] A survey of a large segment of the family of these two patients is in full agreement with the accepted contention that the condition is hereditary.[4]

Methods

The patient was admitted for study in the Metabolic Unit of the Mayo Clinic in November, 1962. A supervised house diet was administered, except during periods when fasting was required. The patient drank two glasses of milk daily to foster adequate intake of calcium and phosphorus.

On the first day, the per cent of tubular reabsorption of phosphate[5] for a 12-hour overnight period was determined to serve as a control, during which time the patient received 1000 ml. of 5 per cent solution of glucose in water intravenously. The formula utilized for the calculations was:

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(Brachymetacarpal Dwarfism)

Endocrinologic
Studies
on
a
Patient

Per cent tubular reabsorption of phosphate =

$$\left(1-\frac{\text{urine phosphate x serum creatinine}}{\text{urine creatinine x serum phosphate}}\right) \text{x } 100$$

On the second night after admission the patient received a continuous infusion of 200 units of parathyroid extract (Lilly) in a solution of 1000 ml. of 5 per cent glucose in water over a period of 12 hours, and the tubular reabsorption of phosphate over this period was calculated. The potency of this parathyroid extract had been previously verified in a normal control individual.

A mock Ellsworth-Howard test was carried out on the fourth day to serve as a control, and an actual Ellsworth-Howard test was performed on the fifth day in the following manner: After a night of fasting, the patient was given 500 ml. of water orally at 7:30 a.m. to ensure adequate urinary flow. At 11:00 a.m. he received an intravenous injection of 200 units of parathyroid extract. Urine was collected hourly from 8:00 a.m. to 2:00 p.m., and the phosphate in each specimen was measured.

During the following week a calcium infusion test was performed as follows: The serum phosphate was determined, and urine was collected hourly from 8:00 a.m. to 12:00 noon for measurement of its phosphate content. Fifteen mg. of calcium per kg. of body weight was administered intravenously as calcium gluconate in 1 liter of isotonic saline during the next eight hours. On the following day, serum phosphate was determined at 8:00 a.m. and 12:00 noon, and urine was collected hourly from 8:00 a.m. to 12:00 noon for measurement of its phosphate content.

Cytogenetic studies were performed and included examination of the buccal smear and chromosomal analysis of the leukocytes cultured from the peripheral blood.

Results

The control values at the beginning of the present study were: 9.6 mg. of calcium, 4.2 mg. of phosphate, 2.3 mg. of magnesium, 15.9 King-Armstrong units of alkaline phosphatase, and 1.2 King-Armstrong units of acid phosphatase per 100 ml. of serum. The concentration of sugar (glucose) was 81 mg., that of creatinine, 0.9 mg., and that of urea, 42 mg. per 100 ml. of blood. The protein-bound iodine was 5.7 micrograms per 100 ml. of serum. The erythrocytic uptake of radioactive triiodothyronine revealed a coefficient of binding of 11.6 (normal: 8.7 to

13.5). At 8:00 a.m. corticosteroids in the blood measured 18.1 micrograms per 100 ml. of plasma, and at 4:00 p.m., 11.6 micrograms. The amount of urinary ketogenic steroids excreted in 24 hours was 9.5 mg., and 11.5 mg. of urinary 17-ketosteroids were recovered in 24 hours. The pituitary gonadotropin assay revealed five rat units, and the estrogen assay, 13 rat units per 24 hours of urine. The basal metabolic rate was −1 per cent.

During the control period, the per cent tubular reabsorption of phosphate was 82.8, while during administration of parathyroid extract it decreased to 70.7. The results of the mock and actual Ellsworth-Howard tests (Table 1) illustrate the slight phosphaturic response induced by the parathyroid extract. The calcium infusion test (Table 2) lowered the urinary phosphate and elevated the serum phosphate values.

The buccal smear was chromatin-negative. Karyotypic analysis of the cultured leukocytes revealed the uniform presence of 46 chromosomes, including a morphologically normal X and Y chromosome.

Comment

Endocrine studies of pseudo-pseudohypoparathyroidism reported in the literature are difficult to evaluate because of the diversity of the cases which have been included under this nosologic term. Pseudo-pseudohypoparathyroidism has been described in association with gout,[6] diabetes mellitus,[7,8] Turner's syndrome,[9-11] hypothyroidism,[8,9] diminished adrenal function,[8] and absence of pituitary gonadotropin in the urine.[8]

TABLE 1
Ellsworth-Howard Test

Time	Urinary phosphate, mg. Mock (control)	Actual
8-9 a.m.	21.9	24.1
9-10 a.m.	10.1	19.7
10-11 a.m.	6.5	21.4
11-12 noon	4.7	26.2*
12-1 p.m.	6.9	32.8
1-2 p.m.	6.8	20.7

*200 Units parathyroid extract administered at 11:00 a.m.

Parathyroid Hormone Responsiveness

The correct evaluation of parathyroid function and parathyroid hormone responsiveness is vital in the differential diagnosis between pseudohypoparathyroidism and pseudo-pseudohypoparathyroidism. The first and most important criterion is that the patient with pseudo-pseudohypoparathyroidism, by definition, can never manifest the clinical symptoms or signs of hypocalcemic tetany, while tetany is common in pseudohypoparathyroidism. The final diagnosis depends on laboratory data. By original definition, serum calcium and phosphorus values must be normal in pseudo-pseudohypoparathyroidism, whereas in pseudohypoparathyroidism, the value of calcium is commonly low and that of phosphate is elevated.

Many authors have emphasized a normal response to parathyroid hormone as a requisite feature of the clinical entity of pseudo-pseudohypoparathyroidism, and yet the original patient described by Albright and associates[2] did not respond to the Ellsworth-Howard test. Among 12 patients undergoing an Ellsworth-Howard test whose cases have been reported, four have responded with apparently significant phosphaturia[6,12-14] and eight have not.[2,7-9,15-18] In our patient, only slight phosphaturia resulted from the parathyroid extract. The erratic response of normal individuals to the Ellsworth-Howard test has been noted frequently. Dent[19] men-

TABLE 2
Calcium Infusion Test

Time	Control (November 25) Urinary phosphate, mg.	Serum phosphate, mg./100 ml.	Test (November 26) Urinary phosphate, mg.	Serum phosphate, mg./100 ml.
8-9 a.m.	10.2	4.0 (8 a.m.)	2.5	5.7 (8 a.m.)
9-10 a.m.	6.0		1.4	
10-11 a.m.	5.9		1.7	
11-12 noon	14.0		1.2	2.9 (12 noon)

tioned a variable phosphaturic response to parathyroid extract in four normal persons, and, for similar reasons, the value of the Ellsworth-Howard test in separating the abnormal from the normal individual has been repeatedly questioned.[20-23] The various explanations for the inconsistent response of normal individuals to parathyroid extracts have included varying potency of the commercial parathyroid preparations,[15] inadequate presence in the extracts of only one of two hypothetic parathyroid moieties, and the interfering effects of normal diurnal variations in phosphate excretion.[19]

Tubular Reabsorption of Phosphate

Perhaps it has not been sufficiently emphasized that phosphaturia is a poor index of response to the parathyroid hormone.[24] One of the factors controlling phosphaturia is the glomerular filtration rate. An increase in phosphaturia may be due merely to an increased glomerular filtration rate,[23] and a bona-fide phosphaturic response may be masked by a lowered glomerular filtration rate. A more significant index of the renal effect of parathyroid hormone is determination of a change in the tubular reabsorption of phosphate. Phosphate is completely filtrable through the glomerular membrane, and the phosphate which is found in the urine is that which has not been reabsorbed by the renal tubules. One of the primary physiologic effects of the parathyroid hormone is control of the amount of phosphate that is reabsorbed by the tubules.[25] Tubular reabsorption of phosphate is the amount of phosphate filtrated by the glomerulus minus the amount of phosphate found in the urine. The filtered load of phosphate may be calculated by the product of the glomerular filtration rate and the serum phosphate.

Thus the tubular reabsorption of phosphate includes three factors which affect or reflect phosphate excretion: urinary phosphate, serum phosphate, and the glomerular filtration rate. The overnight tubular reabsorption of phosphate test before and after the administration of parathyroid extract that was used in our patient was devised by Becker, Purnell, and Jones[26] as a clinical index of endogenous parathyroid activity. Our patient responded in a normal fashion with a significant reduction in tubular reabsorption of phosphate in the period that followed the injection. If the Ellsworth-Howard test alone had been utilized, one would have had to conclude that there was very little response.

Calcium Infusion Test

The calcium infusion test was devised by Howard and co-workers[27] as a method of evaluating parathyroid function. It was reasoned that exogenous hypercalcemia decreases endogenous parathyroid secretion and will consequently diminish urinary phosphate excretion and increase the serum phosphate. The test yields different results depending on the number of hours after the infusion that the blood samples are taken. For example, in our patient, the phosphate value on the morning prior to the calcium infusion was 4.0 mg. per 100 ml. of serum, and on the following morning it had increased to 5.7 mg. By the afternoon of the same day, however, the phosphate value had decreased to 2.9 mg. (Table 2). The variation in the times that blood and urine were collected may explain the inconsistent response of patients with pseudo-pseudohypoparathyroidism to the calcium infusion test.[6-9,13-18]

As an alternate method of demonstrating the normal response of a patient to parathyroid extracts, daily intramuscular injections of the extract for several days, followed by determinations of the serum calcium and phosphorus, have been suggested. A normal response would be characterized by an increase in the serum calcium value and a decrease in the serum phosphate value.[21-23,28]

The relationship between pseudohypoparathyroidism and pseudo-pseudohypoparathyroidism remains obscure, especially since both have allegedly occurred in the same family.[29] It has been claimed that pseudohypoparathyroidism may represent the full expression while pseudo-pseudohypoparathyroidism represents the forme fruste of the same syndrome;[30] but the evidence for such postulation is not incontrovertible.[31,32] Pseudo-pseudohypoparathyroidism is not an endocrine disease, but a "syndrome of multiple congenital defects."[32] However, the appellation is useful because it calls attention to the endocrine disease from which it must be differentiated, that is, pseudohypoparathyroidism.

Summary

Endocrine determinations have been performed on a man with the physical stigmata of pseudo-pseudohypoparathyroidism. Calcium metabolism and phosphate metabolism were studied after parathyroid extract and calcium infusions. A procedure for evaluating the parathyroid hormone responsiveness has been suggested to distinguish pseudohypoparathyroidism from pseudo-pseudohypoparathyroidism, the differential diagnosis frequently being dependent on laboratory data.

Demonstration of the resistance to parathyroid extract in pseudohypoparathyroidism as opposed to the normal responsiveness in pseudo-pseudohypoparathyroidism can be accomplished by the determination of the per cent of tubular reabsorption of phosphate before and after the injection of parathyroid extract. A significant reduction in tubular reabsorption of phosphate in the period that follows the injection will prove normal renal responsiveness and thus further substantiate the diagnosis of pseudo-pseudohypoparathyroidism.

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14-32. Can be obtained with the reprints or from the author.

Order: Let all your things have their places; let each part of your business have its time. — *Benjamin Franklin*

Live as if you expected to live a hundred years, but might die tomorrow. — *Ann Lee*

Acute Lymphangitis and Cellulitis

● Diagnosis ● and ● Therapy

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ACUTE LYMPHANGITIS and cellulitis occasionally complicate both idiopathic and secondary lymphedema and at times occur in patients without permanent lymphedema. The clinical picture may be incorrectly interpreted, and "chronic" phlebitis, recurrent phlebitis, or chronic deep venous insufficiency may be incorrectly diagnosed. The purpose of this presentation is to review briefly the clinical picture of acute lymphangitis and cellulitis and to outline a plan of management.

Clinical Picture

Acute lymphangitis and cellulitis usually are of abrupt onset. Typically, the patient is seized out of good health by prostration, high fever, shaking chills, and profuse sweating. The fever may reach 104 to 105° F. (oral) and attain its peak within one or two hours. Several hours may elapse after the fever appears before the extremity becomes painful to touch. On examination, the patient appears acutely ill and flushed and often is perspiring profusely. Shaking chills are almost an integral part of the picture. The affected extremity appears red and hot and often is tender to touch. The redness may be in streaks indicating the course of the subcutaneous and deep lymphatics, or it may be in diffuse areas not unlike those seen in erysipelas, indicating diffuse cellulitis of the structures through which the inflamed lymphatics course. There may be inguinal or axillary tenderness due to inflamed lymph nodes in these regions. If untreated, usually the acute lymphangitis subsides gradually within a few days, and a feeling of malaise remains. The extremity is painful and swollen for some time after subsidence of acute symptoms. The swelling usually increases with each recurrent episode.

Etiology

Acute lymphangitis and cellulitis may complicate pre-existing lymphedema, or the recurrent infectious episodes may constitute the mechanism by which lymphedema develops. In a review of 131 patients[1] with idiopathic lymphedema seen at the Mayo Clinic, single or recurrent episodes of lymphangitis or cellulitis occurred in 32 patients. Trichophytosis occurred in 11. In a separate study of 80 patients with secondary lymphedema of the leg, Smith and associates[2] found that lymphedema was infectious in origin in 43 patients. In 21 of these, the history of single or repeated episodes of acute cellulitis and lymphangitis was elicited, and in 14 instances there was active trichophytosis. In all 43 patients, acute infection on one or more occasions preceded the persistent lymphedema. While lymphedema of the idiopathic type was complicated by acute lymphangitis and cellulitis in approximately 20 per cent of the patients, only two with lymphedema of the leg secondary to malignancy gave a history of recurrent lymphangitis. This discrepancy undoubtedly reflects the longer duration of the lymphedema in the patients without evidence of underlying malignant disease. Etiologically, streptococci[3-5] are said to be the most common offenders; however, staphylococcus[6] has been incriminated, and dermatophytosis probably has a significant contributing part.[7]

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Differential Diagnosis

Since acute lymphangitis with cellulitis complicating lymphedema is confused most frequently with acute thrombophlebitis, it may prove helpful to reiterate several diagnostic points in the differentiation of these two conditions. The acute onset of fever, chills, and prostration in acute lymphangitis and cellulitis is in contrast to the more gradual onset of symptoms in thrombophlebitis. In thrombophlebitis, fever seldom reaches the degree seen in acute lymphangitis and cellulitis, and chills are absent except in septic thrombophlebitis. On examination, the acutely inflamed red, tender, moderately swollen leg in acute lymphangitis and cellulitis is easily recognized by an experienced observer as differing from the edematous leg in acute venous thrombosis. Acute thrombophlebitis usually causes a discomfort that is deeper in the tissues of the calf and thigh and is more nagging. On examination in acute thrombophlebitis, the tenderness to touch that is characteristic of acute lymphangitis is absent, and there is tenderness to deep palpation of the calf and thigh along the course of the main venous channels. Redness is likewise absent in thrombophlebitis, but the venous pattern is increased because of venous obstruction. This latter finding is characteristically absent in a patient with acute lymphangitis and cellulitis. Finally, in patients who are in the chronic stage of either disease, deep venous insufficiency with its characteristic pigmentation about the inner areas of the ankle and the lower part of the leg, evidence of previous stasis ulceration, current stasis ulcers, atrophy of the skin, venectasiae, and localized varices are easily distinguishable from the hallmarks of chronic lymphedema manifested by a firm nonpitting, diffuse swelling of the leg and foot with the characteristically square toes and a thickened piglike skin. This appearance, of course, during the acute episode, is modified by the superimposed acute lymphangitis and cellulitis. The physician should be constantly aware of the differential diagnosis so that a patient with acute lymphangitis and cellulitis may not only be given proper treatment, but also not be exposed to prolonged, costly, and potentially hazardous anticoagulant therapy as well as the mental trauma which occasionally is inflicted on patients whose conditions have been mistakenly diagnosed as "chronic" thrombophlebitis. Correct recognition of the two conditions will prevent the even graver mistaking of an acute deep thrombophlebitis for acute lymphangitis, with the potential serious and disastrous effects that could follow omission of indicated anticoagulant therapy.

Therapy

On the basis of our preliminary[8] and subsequent experience, we have evolved the following plan for treatment of patients with acute lymphangitis and cellulitis. Whenever possible the patient is hospitalized and placed at bed rest so as to minimize movements of the affected extremity. Bathroom privileges are allowed in preference to the use of bedpans. The severe pain during the acute episode may require administration of sedatives or mild analgesics, and salicylates will often afford symptomatic relief.

Antibiotic Therapy

The most important factor in the treatment of a patient with acute lymphangitis and cellulitis is the immediate administration of proper antibiotic therapy. In patients who are not sensitive to penicillin, we give 600,000 units of procaine penicillin G twice daily, and this dosage is continued for 24 to 48 hours after the patient has been completely afebrile. In patients sensitive to penicillin, erythromycin is given in a 250-mg. dose every four hours initially; after the temperature has subsided this dose is given every six hours. This alternate regimen is likewise continued until the patient has remained afebrile for 48 hours. In addition, warm, moist compresses to the extremity often give symptomatic relief from the discomfort of the inflamed skin involved by the acute cellulitis. Once fever has subsided, the patient, using a proper elastic support, is allowed out of bed; this elastic support can be in the form of Ace bandages, a 100-per cent para rubber bandage, or more recently a made-to-measure foot-to-knee Jobst stocking. Five milligrams of a thiazide diuretic such as bendroflumethiazide (Naturetin) given every other day may also aid in control of edema. When this is done, urea in the blood and potassium in the serum should be checked periodically.

Long Term Prophylactic Therapy

In our opinion, any patient who has had one or more episodes of acute lymphangitis and cellulitis and who has lymphedema of the extremity is a potential candidate for intermittent long-term antibiotic prophylaxis. We have customarily prescribed benzathine penicillin G in amounts of 1,200,000 units administered intramuscularly once a month or phenoxymethyl penicillin in amounts of 250 mg. four times daily for five to seven days of each month. In individuals allergic to penicillin, erythromycin, in a dose schedule indentical to that employed for phenoxymethyl penicillin, is prescribed. Our results to date have been gratifying, and to most patients the resulting freedom from recurrent and incapaciting episodes of acute lymphangitis and cellulitis, as well as the prevention of progressive lymphedema, has constituted ample reward for the small inconvenience in time and expense posed by the long-term antibiotic program.

Treat Associated Dermatophytic Infection

In addition to the program of antibiotic therapy and to the use of proper elastic support, the patient with recurrent lymphangitis and cellulitis should be carefully examined and treated for any associated dermatophytic infection. We instruct patients in the proper hygiene of feet and in the application of an appropriate antifungal agent such as triacetin ointment and powder. In selected patients, we have resorted to the administration of griseofulvin in the hope of eradicating the fungal infection and thus eliminating a portal of entry for the organism responsible for the repeated episodes of lymphangitis and cellulitis. Finally, in those patients with postmastectomy lymphedema, proper physiotherapeutic measures as described by Stillwell[9] for the care of the arm should be employed.

Summary

Acute lymphangitis and cellulitis is not an uncommon disorder. Physicians should be aware of the differential diagnosis between acute lymphangitis and cellulitis and acute deep venous thrombosis. Acute lymphangitis and cellulitis either may complicate lymphedema of the idiopathic or secondary type or may occur de novo, eventually giving rise to infectious lymphedema.

The treatment of choice is the administration of proper antibiotic therapy during the acute phase in conjunction with bed rest and symptomatic measures.

The long-term management of the condition consists of intermittent antibiotic prophylaxis and the use of proper elastic support, supplemented at times by the intermittent use of a thiazide diuretic and treatment of dermatophytic infection, if such is present.

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A Tribute to Hippocrates

We physicians revere Hippocrates because he was the first man to teach, first, that many diseases clear up best if the physician does not meddle too much, and, second, that medicine can advance only when it breaks away from magic. Gradually, through the two milleniums before the birth of Christ, physicians had been coming to see that some diseases are due to injury and contagion and the wearing out of parts, but so far as we have a record, Hippocrates was the first to go the whole way and state that no disease is purely miraculous in origin.

And if through the ages, religiously minded people had only listened to Hippocrates and had given his successors the freedom to dissect, to perform autopsies, to experiment on animals, and to report honestly and fearlessly what they found, how almost certain it is that today medical knowledge would be hundreds of years ahead of where it is, with tuberculosis and cancer and arthritis perhaps only memories of the past. (Walter C. Alvarez)*

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*Rapport, Samuel, and Wright, Helen: Great Adventures in Medicine. The Dial Press, New York, 1952, p. 24.

To overthrow superstition, to protect motherhood from pain, to free childhood from sickness, to bring health to all mankind: These are the ends for which, through the centuries, the scholars, heroes, prophets, saints and martyrs of medical science have worked and fought and died. — Yandell Henderson

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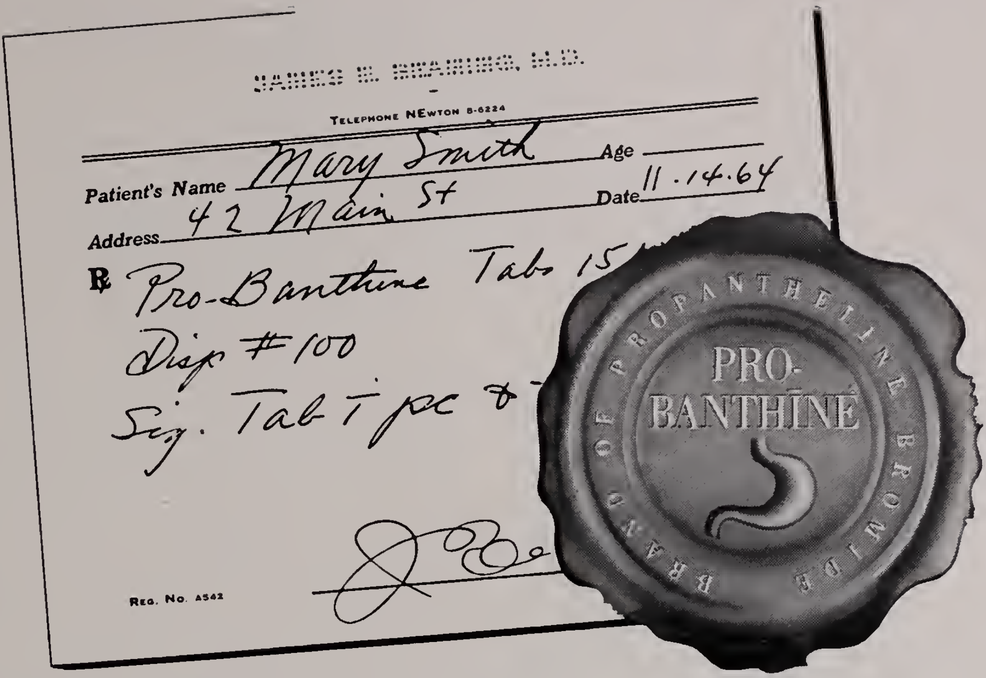
On either side of the river, was there the tree of life, which bare twelve manner of fruits, and yielded her fruit every month: and the leaves of the tree were for the healing of the nations. — Revelation XXII, 2



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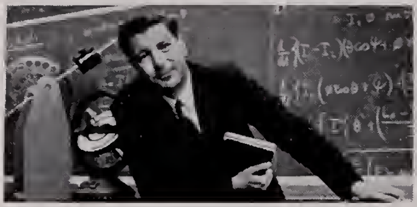

Stoll[1] used the drug in 50 patients with anxiety, and noted: "There was no drowsiness in this group of patients and, because of their alertness and less impaired concentration, they were able to continue with and, in some cases, return to their daily work."

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Before prescribing, see SK&F Product Prescribing Information.

Photograph professionally posed.

1. Stoll, L. J.: The Use of Trifluoperazine ['Stelazine'] in General Practice, M. Press *243*:578 (June 29) 1960.

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Editorials

A Triumph of Organ-Grafting Technique and Its Moral Problems*

SENSATIONAL INDEED are the journalistic accounts of the most recent challenge to surgical skill in devising successful organ transplantation, but seldom do these publicity releases complete the public case records. The full story, with all its obsessive drive, anxiety, frustration, heartache, and often tragedy, can only be surmised.

Some idea of the problems in the otherwise optimistic picture may be obtained from comments such as those of Joshua Lederberg, the distinguished Nobelate geneticist, who has philosophically scanned the situation, or of J. Russell Elkington, who has painstakingly reviewed two hundred and forty-four reported kidney-transplant operations. Both Lederberg and Elkington raise questions about the moral problems, which the triumphs of surgical technique cannot dodge.

In a remarkably clear manner Victor Cohn has discussed some of the ethical problems which may be involved. The relation of these problems to "medical ethics" is not so much concerned with medical etiquette between members of the medical profession as it is with the more basic morality which lies at the base of the patient-doctor relationship.

Historically the current situation is somewhat analogous to what happened in the 17th century, when blood transfusion was first undertaken as a practical clinical procedure in an effort to apply William Harvey's 1628 demonstration of the blood circulation. The attempts failed tragically, because of technical ignorance. The moral problem then was clear: one could not undertake blood transfusion without the risk of death, and the effort was condemned by social fiat. Two centuries were required to surmount the technical problem. It was only after Karl Landsteiner (1868-1943) revealed the factors operating in the incompatibility of blood groups, that transfusion gradually became a successful and socially approved procedure.

In the current situation in organ transplantation it seems likely that technical understanding and skill will triumph much more rapidly than was the case with blood transfusion. On the other hand, it appears that the moral problems involved may multiply.

Stanford University's Nobel Award geneticist, Joshua Lederberg,** asks such searching questions as:

> "When surgeons are able to transplant hearts, who will choose which dying patients get the new ones? Who will decide whether the organs of a dead person should be transplanted directly or maintained in frozen storage, and who will decide the price?"

Continued

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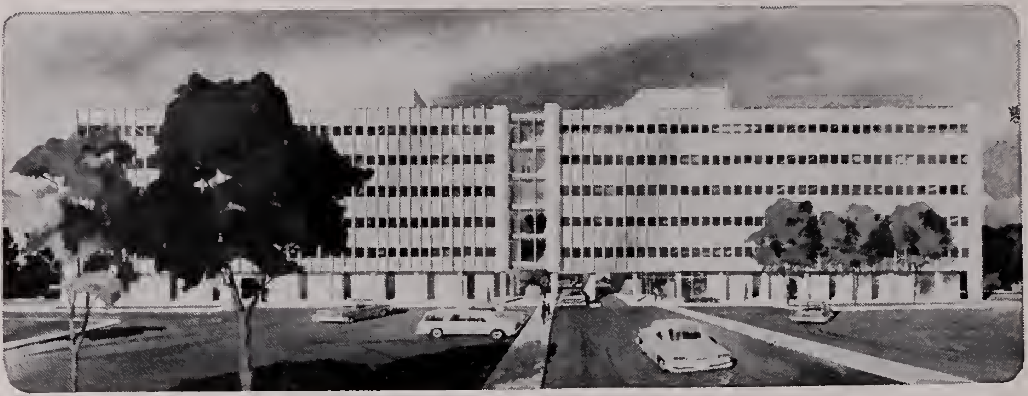
*Presented at the Minnesota State Medical Association Annual Meeting in Rochester, May 18, 1964.

**The new scientist.



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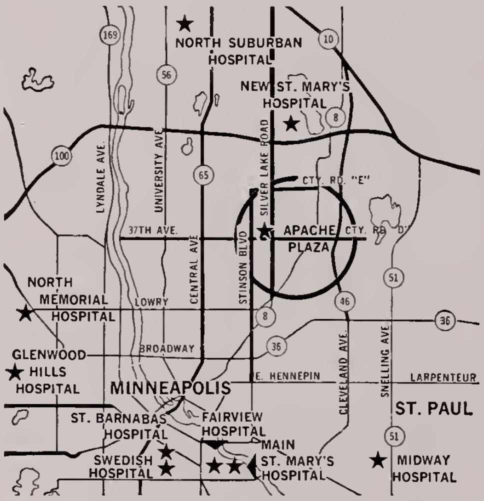
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Lederberg points out that the transplantation of hearts, livers, and even complete limbs may be relatively easy within the next twenty years. The moral problems raised by the potential success of these efforts are as serious in other parts of the world as with us.

Lederberg concludes that the future of organ transplantation, which may even include gonads with resulting benefits, may result in serious controversy. All parents may be expected to insist that their children be given the intelligence of genius. Who will decide how to use this genetic pool? These problems are too important to be entrusted merely to biomedical scientists or to members of the health professions. There must be careful and detailed public study of these matters, with solutions dependent upon moral, social, and economic factors, and most importantly, upon enlightened public opinion.

Elkington, in reviewing several hundred kidney transplantations, finds increasing survival periods for recipients as technical skill improves. Chances of surviving a year are now about 75% for patients who get a kidney from a close relative. However, the moral problem remains: *is this life extension of the recipient worth the potential reduction in the life span of the donor?* Many factors must be considered in the decision: relative ages, potential productiveness, relative contributions and value to the community, and individual consciences. As Victor Cohn indicates, it is to the lasting credit of the health team personnel that these considerations are carefully weighed and all aspects of the case fully explored before the team decides to let nature take its course or, on the contrary, to intervene.

Technique and Reason

Technical surgical skill already seems available. The major current block is immunological, relating to the process of rejection. With the use of mercaptopurine compounds to block antibody formation, and with radiation of the spleen to further reduce the appearance of rejection factors, it seems that experimental study will soon result in successful applications to clinical practice in organ transplants. However, much judgment will be required in control of the immunological inhibition. Blocking the immunological factors must not be achieved at the risk of interfering with the long-range welfare of the recipient of the transplant.

It now seems well established that kidneys may be successfully transplanted from one identical twin to another. But how many of us have altruistic identical twins handy, if one of our kidneys goes wrong? Or suppose I were the healthy twin: would I be ready to part with one of my kidneys for the benefit of my twin, never to regret my action?

A two-way responsibilty exists: if I am the healthy person and wish to be generous, would I be wise to sacrifice one of my healthy organs if I had heavy family responsibilities? If I am the sick one, would I be justified in calling on even a close relative to yield a healthy organ for me, merely to keep me alive for another year or so?

The ethical issue for the donor is slight: self-sacrifice is commended for generosity and for social welfare. Yet self-sacrifice is not always justifiable even on the basis of social expediency, let alone enlightened self-interest. From the standpoint of the recipient it does not seem that anyone has the right to expect that someone else would willingly give up some part of his body for the recipient's benefit or even his life. The problem is complicated by our sentimentalized fear of death. Few of us have disciplined ourselves to face death with dignity and resignation when our time comes.

A Scientific Approach to the Ethical Problem

The ethical problem is not then satisfactorily answered by reference either to hedonism* or to Platonic idealism:* the two ancient and conflicting theories of justifying human conduct, which are still being debated. Nor will help come by referring to the 19th century compromise of pragmatic utilitarianism, the idea of the greatest good for the greatest number. Some light may be found, however, in exploring the consequences of evolutionary principles from the

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*See Test Your Word Score Page 211.

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basis of Warner Fite's naturalistic individualism. Actually, ethical theories have lost contact with the realities of today, and philosophers have failed in communication with us, just when we need them most.

There is, however, a pragmatic scientific approach to the problem of our motivation and conduct. *This requires full self-consciousness and both intellectual and emotional honesty: traits, unfortunately, not well cultivated among us.* I am referring to a moral approach to living on the basis of an understanding of the complex factors involved in maintaining desirable interpersonal relationships.

The relationships between individuals or between groups of individuals are delicately poised on many intangibles; however, some generalities are emerging. As agreed upon a couple of decades ago by a number of distinguished biologists and philosophers, it is possible to express a naturally operating principle governing human relationships in scientific terms, that is, in a manner compatible with biological laws of adaptation and survival. This principle may be considered to be naturally operative in the sense that it continues to be effective whether we are conscious of it or not, or whether we like it or not.

Ethicogenetic

This ethical principle, as stated a quarter of a century ago, in a discussion which I called "Ethicogenesis," is: The probability of the survival of a relationship between individuals or groups of individuals increases with the extent to which the relationship continues to be mutually satisfying.

What does this ethicogenetic principle mean in organ transplanting?

First, there is *the patient,* anxious, trying to repress the unpleasant contemplation of death, and yet appalled at the sudden responsibility of accepting something truly valuable beyond price from someone else. Yet for every ordinary patient, even if he is well self-disciplined, there is the will to live at any cost. This is essentially the quintessence of hedonism.

Second, there is *the surgeon,* on the surface cool, calm, collected, self-reliant in technical skill, troubled only by the possibility of failure through lack of knowledge and experience of how to control the immune processes in probable rejection, and also concerned over the delicacies of obtaining a suitable and willing donor. He represents the pragmatic utilitarian.

Third, there is *the donor,* often over-eager to sacrifice because of some subconscious guilt complex, or simply happy to give something truly important for a loved one. Here is the personification of Platonic idealism, on which our acceptable Judeo-Christian ethic is based.

One might think that this categorization covers the interpersonal relationships involved in organ transplantation. However, the situation is vastly more complex, as a moment's reflection will reveal.

Consider, for example, the somewhat related matter of blood transfusion, now under socially acceptable methodology, but with continuing difficulty in obtaining donors in spite of every inducement. Or consider the more emotionally charged problems of artificial insemination, which are still under vigorous social debate. In these instances the technical aspects of the situations have been adequately and successfully solved; and risks to the living are minimal. This is not the case, however, with organ transplantation.

There remains the high probability, in spite of sensational publicity, that an organ transplant will be rejected. In this case the recipient is clearly as badly off as ever, and the donor is worse off. The recipient may have gained a few more weeks of life, but how about the potential reduction in the fullness of living for the donor? And what profit to the surgeon, except the dubious publicity for the attempt, with soft-pedalling of the failure? This all lacks the clean smell desirable in the health professions.

The establishment of socially acceptable organ banks might reduce some of the moral difficulties inherent in organ transplantation, but the technical problems are as yet unsolved. Even donation of organs after death to an organ bank might have complications. There might also be difficulties for recipients

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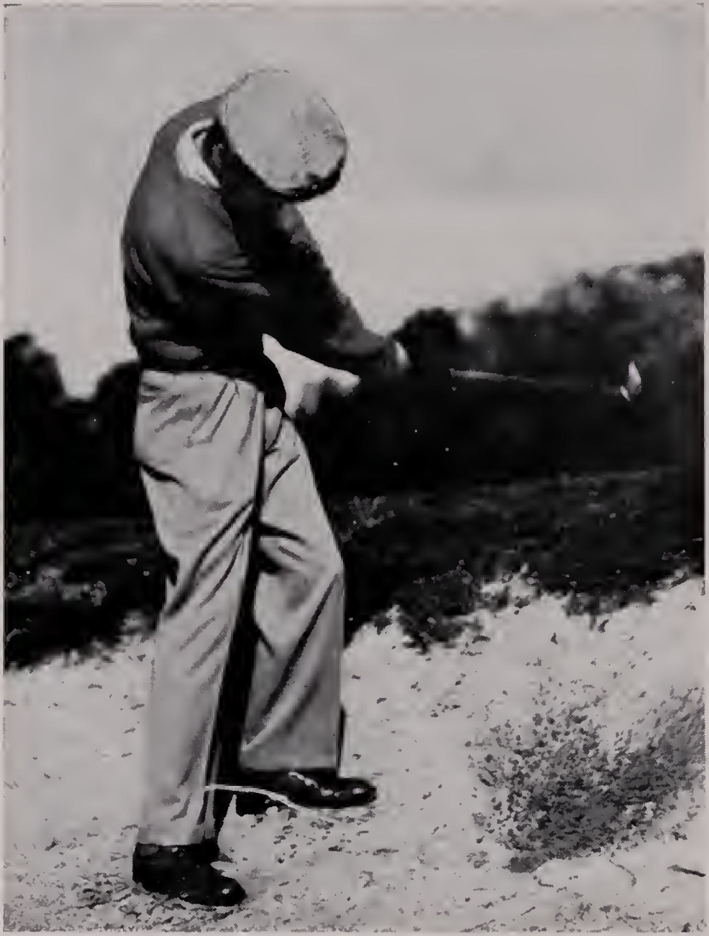

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as a result of emotional factors in the anonymity of the donor. Perhaps these matters may be more satisfactorily solved by utilizing mechanical devices for functional purposes, as is possible in kidney failure and in amputations. Indeed, some brave biomedical scientists are busily experimenting with artificial hearts, and some cardiovascular devices have already been successfully developed for application clinically. Here technique may truly triumph with relatively little fear of ethical complications.

Psychosocial Factors

Further to be considered is the overwhelming complex of the psychosocial factors involved, not only with respect to the three principles in the organ-transplant drama, but also in regard to the social environment in which each respectively moves, and in the larger environment of the whole community. It is doubtful that harmonious interpersonal relations between recipient, donor and surgeon, and between these and their respective communities, can be maintained under the harsh realities of probable failure and inevitable death. In anticipation, these interpersonal relations seem so pleasant and promising, but the mutual satisfactions necessary for the survival of harmony are often too delicately balanced to last.

If those who are enmeshed in the particular interpersonal relationship under consideration wish it to continue, then it is clearly incumbent upon each to do what is possible to make the relationship satisfying to the others involved in it. This requires calm, honest, and open discussion among the recipient, the donor, and their respective families, under the leadership of the surgeon, and with the guidance of religious advisors.

Ethical Responsibility of the Surgeon

Here, then, are the ethical responsibilities of surgeons in organ transplantation: (1) to undertake nothing until the technical procedures are fully under control, including the as yet unsolved immunological problem of transplant rejection; (2) to discuss the whole matter carefully and in detail with prospective recipient, proposed donor, family and religious advisors; (3) to be well versed in ethical theory and in psychology, so that individual motivations can be detected, exposed, and discussed, and (4) to be prepared to do everything possible to maintain harmonious interpersonal relations among recipient, donor, family and religious advisor, no matter what the outcome of the endeavor may be.

The *moral problems of organ transplantation* are not the exclusive responsibility of surgeons or of biomedical scientists who may be working on the technical details which must be solved for clinical success. Nor are they the primary responsibility of prospective recipients or donors. They *are the responsibility of all intelligent people.*

It would be wise for biomedical scientists and members of the health professions to have no false pride or intellectual arrogance about the matter. It would be expected that these intellectual leaders would examine their own individual motivations and get acquainted with the rudiments of ethical theories and their historical development. Also they would be wise to remember that among the consequences of biological evolution and its basic principle of harmonious adaptation for survival, is the proposition that the probability of survival of relationships between humans, as individuals or as groups, increases with the extent to which these relationships are mutually satisfying.

Chauncey D. Leake, Ph.D.*
San Francisco, California

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*University of California Medical School.

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*Chupkovich, V.; Finnerty, F. A., Jr., and Kakaviatos, N.: The value of chlorthalidone plus reserpine in moderately severe and severe hyper tension: A two year study. Presented at the 7th Inter-American Congress of Cardiology, Montrea June 14–19, 1964.

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One of the handicaps in the X-ray examination of the chest results from the use of one film and one exposure for the entire thorax from apex to base, although there are striking differences in thickness and density of the different portions of this area. Ideally, we should make at least four different exposures, in order to equalize these differences. A second impediment is occasioned by large areas of the lung which are covered by denser parts such as the ribs and mediastinal structures. However, such difficulties can be compensated for in a variety of ways. The importance of the lateral view has been demonstrated not only in determining the location and distribution of a lesion which is known, but also in finding an abnormality which may not be visible in the posteroanterior view.

In addition, the X-ray examination of the chest may require various oblique projections, the apical lordosis, and the posteroanterior lordosis views. Structures which are not clearly visualized in one position may become apparent in another. Pulmonary infarcts not clearly visible in the conventional positions may be demonstrated when certain oblique projections are used. The same would apply to many other pathological processes.

In the effort to overcome the handicap of the varying degrees of radiographic density in the thorax resulting from the chest wall, the mediastinal structures, and other dense areas, techniques utilizing highly penetrating radiation are now in use. Such films tend to give a gray appearance and do not exhibit the striking contrast of black and white which characterizes chest roentgenograms made with low voltage radiation. This has led many physicians who are not fully aware of the physical factors and the diagnostic difficulties of chest examination to be critical of such films. But the fact is that these films are of much greater diagnostic value than the high contrast film. Experimental studies are under way using radiation factors which are equivalent to 6,000,000 volts; such films demonstrate structures in the mediastinum hitherto scarcely observed. Such techniques are limited in usefulness, however, because apparatus of such power is not generally available.

The radiographic examination of the chest in the symptomatic patient, as conventionally practiced, represents a screening procedure. Beyond this a number of other methods should be undertaken to determine more definitively the anatomical location of the abnormality and its exact nature. These methods include over-exposed films using a grid diaphragm, a variety of positions, and varying degrees of exposures. In addition the use of body section roentgenography, (tomography or planigraphy) may be most helpful, but this procedure is not used widely enough. By this means the structures surrounding any particular area may be blurred out sufficiently so that the shadow of the disease process or of an air-filled bronchus will stand out vividly. In most cases abnormalities of the major bronchi, especially tumors, can thus be clearly revealed. Furthermore, cavities in the lung, small nodules, as well as many other conditions can be more clearly delineated; in some instances lesions not seen in the ordinary roentgenogram become visible. For the demonstration of the segmental bronchi, bronchography with contrast medium should be used. Finally, the pulmonary blood vessels may now be readily demonstrated by injection of contrast medium either intravenously or by catheterization directly into the pulmonary artery. In recent years efforts have been made to delineate the bronchial arteries with contrast. Such a procedure could be of great value in differential diagnosis, especially of tumors and other such chronic processes. The demonstration of the azygos vein can be accomplished readily by injection into a rib of con-

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trast medium, and in rare situations this may improve our diagnostic acumen.

All of the above procedures are applicable to the patient with symptoms in whom a specific lesion is likely to be present. The roentgen examination of the asymptomatic individual, whether during a mass survey or individually as a part of a routine examination, presents a different problem. It is obviously impractical to undertake such elaborate procedures when the probability of discovery of a lesion is relatively small. Commonly only one posteroanterior view is made under these conditions. If it were possible, as it should be, to use two films for a routine examination, I believe stereoscopic posteroanterior views would be the best procedure. The chief errors in such routine examinations are the failure to detect the early lesions of tuberculosis, very small tumors, or other minimal pathology. Such errors are due to superimposition by overlying structures, especially the ribs; the shift in position in two films made with the X-ray beam at different angles tends to overcome this handicap. If three films were available, obviously, stereoscopic posteroanterior and lateral views would be the best.

Finally, I would urge that the technique of chest X-ray examination be given close attention and consideration by all those who are using it. It is much too valuable a procedure to be attempted casually. Our sins of omission, our failure to recognize small or early lesions in the lung, are clearly apparent to anyone who has studied the previous roentgenologic history of many patients. A large part of these failures is due to poor technique. The roentgen detection and identification of pulmonary disease processes, especially when the lesion is early or small, are difficult enough. It is inexcusable that we should add to these difficulties by inadequate use of the technical facilities available to us.

Leo G. Rigler, M.D.*
Los Angeles, California

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*Professor of Radiology, University of California.

Methuselah,* Here We Come!

The word generally out of Washington is that President Johnson expects some pretty fast action on Medicare* when the eighty-ninth congress assembles.

Whatever the merits of Medicare, as the politicians have been describing it, they can get out of it perhaps the greatest patronage bonanza since the government got into running the country's farms. A vast array of bureaucrats will be needed to administer it, and, of course, only party faithfuls can qualify.

But what about the old folks who are supposed to benefit? If we believe the politicians, life after 65 will be a breeze — no more doctor bills, no more hospital bills, no more drug costs, no more service costs. Our seniors can have full hospital care, doctors and nurses swarming about to wait on them hand and foot, with free pills and medicine so long as there still is breath in their old carcasses.

It's a wonderful filial thought. Folks who languished through to their 65th birthdays can practically be made over and, with Medicare at hand, outlive Methuselah. In addition, their offspring can furtively gloat that they won't need to chip in for a new set of store teeth, new eyeglasses, or special shoes. Their senior kinsfolk, if we believe the politicians, will actually enjoy being laid up, since the best of everything will be theirs, along with the comforting thought that the government will pick up the whole tab.

Medicare is mainly a hospitalization plan aimed at taking over an exist-

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*See Test Your Word Score Page 211.

Continued

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ing free enterprise activity. But it has numerous tricky provisions about hospital care that may cost the old-timer, or his heirs, a lot of money if he doesn't guess right about how long he'll need hospitalization. No matter what his ailment is, he'll have to share a room with others or pay the difference. Any service he needs beyond what the hospital can provide under Medicare, he'll pay for himself.

He'll have to pay his own doctor bill, also the cost of a private or special nurse's services. No matter how small the print seems to be getting in his home town newspaper, Medicare won't provide him with glasses. Nor will it provide store teeth or a cane.

Like all other government "public service" activities, Medicare is strictly a bureaucratic undertaking, relegating to arbitrary officials the decision as to how we should get sick after 65. And the heck with him who can't fit into their schedule!

We might well ponder on what would have happened had Medicare been in force in Methuselah's time!

Orlin Folwick
Minnesota News Features

The Editor's Soliloquy

Therapeutic Meditation

Is reminiscing a contributing factor in the successful adaptation to advancing age? The studies of McMahon and Rudick* indicate that the depressed oldster who does not recall the past dies significantly sooner than the nondepressed one who indulges in retrospective soliloquy. It was even suggested that reminiscing is of therapeutic value and does not necessarily denote senility.

Between the reminiscer and the reminiscee there operates that subtle, psychological mechanism — the personal equation.** Who has not as a child sat enthralled at a grandfather's knee, glimpsed alluring vistas into the past, traversed their full length, dissolving the barriers of space and time, and then and there relived vicariously some magically resurrected incident, tragic or comic, heroic or humble — a never-to-be-forgotten adventure. Perhaps therein lies the secret formula for the special rapport so often felt between the two alternate generations. Surely the rare value and nostalgic charm of such reminiscence cannot be challenged.

Rather than constituting boredom ad nauseam, pleasurable recollections can for both participants be a profitable and intimate sharing of a bygone experience in the warm afterglow that suffuses all memorable past events. It can be a desirable recreation, however, only when indulged in moderately and not to the exclusion of constructive participation in the present and the future; for the oldster has much to contribute to both time dimen-

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*McMahon, A. W., and Rudick, P. J.: Archives of General Psychiatry. 10:292, 1964.
**See Test Your Word Score Page 211.

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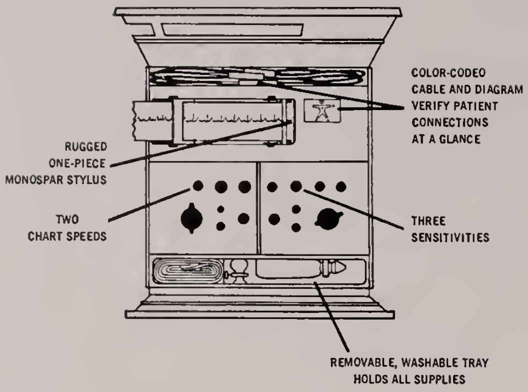
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sions — due to the perspective, insight and wisdom derived from long experience as spectator, auditor, and actor in life's little mime.*

Reminiscing, like confession, may be good for the soul. — C.O.R.

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*See below.

Test Your Word Score

The Editors have picked difficult words from the manuscripts contained in this issue and list them below with their definitions. Test Your Word Score! If you know all nine words and their meaning, you have superior intelligence. If you find you know only six, you still have excellent intelligence; five, good, and four, fair. However, a score of three and below, rates only a "poor."

Watch for the asterisks in the manuscripts each month and test your word sense!

For your Word Score:

Teratogenic — capable of combining to form congenital abnormality. (page 175)

Totipotency — blastomers capable, when isolated, of becoming a complete embryo (first few days of cell division). (page 176)

Hedonism — the doctrine that individual pleasure or happiness is the highest good. (page 199)

Platonic idealism — the theory of the dominance of the ideal element in reality. (page 199)

Methuselah — a Biblical patriarch who — reached 48 score and nine years instead of three score and 10. (page 207)

Medicare — a bureaucratic patronage bonanza. (page 207)

Personal Equation — the emotional and spiritual rapport between two individuals. (page 209)

Mime — a character play of everyday life. (page 211)

Multifarious — having great diversity or variety. (page 247)

Wisdom is knowing what to do next; Skill is knowing how to do it; and Virtue is doing it. — David Starr Jordan

To be born a gentleman is an accident, but to die one is an achievement.
— H. P. Kaye

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Curbstone Consultation

Valvular Heart Lesions

QUESTION: How safe is open-heart surgery for valvular heart lesions?

ANSWER: This is a difficult question, but in general the open-heart valvular surgery falls into the reconstructive and replacement types. The mortality and morbidity is of a higher magnitude for operations upon the aortic valve than upon the mitral valve. Mitral valvular surgery of the reconstructed type has a probable over-all mortality of between 10 and 15%. Valvular replacement surgery has a slightly higher mortality in over-all figures. Aortic valvular reconstructive and replacement surgical procedures has a mortality that varies widely from one cardiac center to another. The mortality figures range from as low as 10% to as high as 50%. It is, therefore, difficult to pick an average figure, but certainly the mortality must range from 25 to 30% as an average over a long series of cases at the present time. In part, the mortality is not due to the surgical procedure itself, but to complications in the cardiopulmonary and renal systems. Also the status of left ventricular myocardium in aortic valvular disease may be much more compromised than in mitral valvular disease. In all fairness to the surgeon one must equilibrate the prognosis of patients with severe aortic and mitral valvular disease in terms of longevity and invalidism as compared to the postoperative status especially in prosthetic valvular replacements of those patients who survived the procedure. Although experience has not been long in terms of years, it has been sufficient to indicate that individuals who survive resume fairly normal lives.

Bacteriology of Bronchitis

QUESTION: Do you think the sensitivity studies of the coughed-up specimens are satisfactory as a guide for effective antibiotic therapy?

ANSWER: We have long felt that a bronchoscopic specimen yields more valid bacteriologic data than a coughed-up specimen contaminated with mouth organisms. If bronchoscopy is not possible, the best alternative would be either tracheal aspiration or the collection of a specimen of coughed-up sputum at the bedside so that the physician could be reasonably sure that the specimen came directly from the bronchial tree and was sent to the laboratory promptly, as are the bronchial secretions collected at bronchoscopy.

David H. Waterman, M.D.
Knoxville, Tennessee

Hardening of the heart ages people more quickly than hardening of the arteries.
— Mutual Moments

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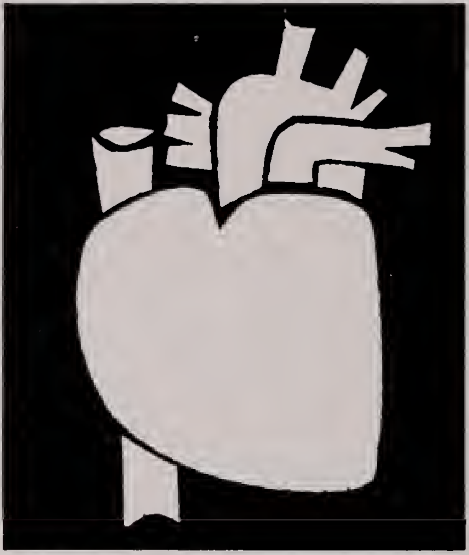

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Fracture–Trauma Conference

Regional Anesthesia in Children with Extremity Injuries

The anesthetic management of children with fractures can sometimes pose more dilemmas and problems than the surgical management. This is particularly true in the case of the child with a full stomach and a recently fractured extremity. In order to illustrate the important points of management, it will be more meaningful to describe the usual practice of one center rather than to describe one case; for one anesthetic success is not evidence of anything except, perhaps, a certain degree of luck.

Early reduction of a fractured arm in a child with a full stomach can be accomplished safely only with a regional anesthetic. The vomiting and aspiration associated with general anesthesia are a leading cause of anesthetic deaths in children and must be avoided. One must choose, therefore, whether to perform a regional block at once or to wait for the stomach to empty and use a general anesthetic. Our practice is to rely on a regional anesthetic and immediate reduction.

Prerequisites for Success

1. Adequate premedication at least thirty minutes before the block is attempted. Secobarbital 1 mg. per pound plus meperidine 0.5 mg. per pound of body weight given intramuscularly is usually adequate.
2. A calm, unhurried atmosphere.
3. Precise technique with proper equipment.

Children of all ages will accept a brachial plexus block if they are well premedicated and gently approached. The intended procedure must be described as part of the treatment that "will make the arm well." The child with a fresh fracture will, in fact, accept the block more readily than a child coming for elective surgery. He is anxious to have the arm fixed and the pain stopped. He looks to the doctors for help and will usually accept the needle as part of the treatment.

Axillary or Supraclavicular Approach

Drugs of choice are lidocaine 1 percent, to which may be added tetracaine to make a 0.1 percent concentration if a prolonged effect is required. Either the axillary or supraclavicular approach can be used. Performing the block

Continued

by the axillary approach causes the patient less discomfort because one need not elicit a paresthesia in order to find the nerves, as is necessary with the supraclavicular approach. However, the supraclavicular block is more reliable, lasts longer and produces a more profound anesthesia. The choice of the approach will, therefore, be influenced by the requirements of the surgeon and the experience and preference of the anesthesiologist.

Finally, after the block is performed, everyone should be prepared to wait for the anesthetic to take effect. There is no escape from this. To try prematurely to reduce a fracture will cause the patient to lose faith in the block. If the child is once hurt by the manipulation, he will tend to interpret all sensations, such as pressure and pulling as painful. Additional doses of a narcotic or thiopental can be judiciously used if the patient is still apprehensive, but sedation should stop short of depressing the laryngeal reflexes.

Advantages and Complications

The advantages of this method are that it avoids three major causes of anesthetic deaths in children, i.e., hypoxia, toxic depression of the cardiovascular system by general anesthetic agents, and vomiting with aspiration.[1] The main complication of a brachial block is a toxic reaction from the local anesthetic agent. This can be avoided by limiting the amount of drug to the maximum safe dose and by avoiding intravenous injections. The incidence of pneumothorax following supraclavicular brachial plexus block has been reported as 0.66 percent and 2 percent.[2] Separate figures for children are not available, but in our experience with children it has been a rare occurrence. The incidence of postanesthetic neuropathy due to the block is also extremely small and is not a significant factor in the choice of an anesthetic.

Van S. Lawrence, M.D.
Hennepin County General Hospital

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Parable of the Isms

Socialism: If you have two cows, you give one to your neighbor.

Communism: If you have two cows, you give them to the government and then the government gives you some milk.

Fascism: If you have two cows, you keep the cows and give the milk to the government; then the government sells you some milk.

New Dealism: If you have two cows, you shoot one and milk the other; then you pour the milk down the drain.

Nazism: If you have two cows, the government shoots you and keeps the cows.

Capitalism: If you have two cows, you sell one and buy a bull. — Anon

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Remember when they called a cigaret a coffin nail? And it was a joke?
— Changing Times

Tumor Conference

Problems in Diagnosis and Management in Carcinoma of the Bile Ducts

When a patient develops jaundice of an obstructive nature, the physician is often presented with a difficult diagnostic problem and a therapeutic challenge, as evidenced by the following case report:

Case History

A 39-year-old white female entered the University of Minnesota Hospitals for the first time on June 19, 1964, with a chief complaint of progressive painless jaundice of one-month duration. Two years prior to admission (April 1962) the patient underwent the first of five operative procedures for a similar complaint. *At that procedure, a firm mass was palpated in the hilum of the liver at the bifurcation of the common duct.* This tumor resulted in obstruction of the right hepatic duct, but the left hepatic duct remained patent. A long limb #10 T tube was inserted into the left duct, the obstructing mass biopsied and a cholecystectomy performed. Pathologic examination revealed chronic cholecystitis with cholelithiasis, and the mass was interpreted as showing ectopic islands of biliary mucosa in dense inflammatory fibrous tissue. It was thought to be inflammatory reaction and not malignant.

Second Operation

The patient apparently improved for a short period on continual bile drainage and was re-explored on August 3, 1962, with the plan to resect the mass. The hilar tumor had, however, enlarged and extended into the right lobe of the liver and was considered at that operation to be unresectable. By this time the left hepatic duct appeared to be invaded, but could be dissected free. A portion of the duct was resected and an end-to-end anastomosis was made to the common duct over a multi-perforated #10 catheter. *Again biopsy was interpreted as ectopic biliary mucosa.* The patient suffered general malaise following this procedure and in March, 1963, developed chills and fever, without evidence of increased jaundice.

Third Operation

After a brief course of antibiotics she improved, and on March 21, 1963, she was re-explored for the third time, again contemplating resection of the tumor mass because malignant diagnosis had not yet been reported. Dissection in the hilum of the liver revealed no extra or intrahepatic duct on the right side even after resection of the tumor high into the liver parenchyma. A cannula was again threaded into the left duct and fixed in place for total biliary drainage. Histologic interpretation of the resected specimen for the first time was reported as a *well differentiated adenocarcinoma.*

Fourth Operation

The left hepatic-duct biliary diversion allowed the patient to remain well until September, a period of six months, at which time the drainage tube was accidentally removed. Jaundice with pruritis ensued, and on November 1, 1963, the patient underwent her fourth surgical exploration. The tumor had recurred locally, had attained a

Continued

size of 2 x 3 cm., and had invaded the duodenal wall and peripancreatic region. Enbloc resection was performed, requiring removal of a portion of the wall of the duodenum. At this time, both bile ducts were located and a limb of a Y tube was placed in each duct. The long limb was placed into the duodenum and the duodenum sutured to the liver capsule around the hilum. The T tube was brought out through the separate opening in the duodenum for external drainage. At the time of this operation, the patient was in her fifth month of pregnancy. Postoperatively she improved and in March, 1964, underwent a spontaneous normal delivery.

Fifth Operation

In June, 1964, she was admitted for the first time to the University of Minnesota Hospitals. By this time, bile drainage had quantitatively decreased, jaundice had progressed, there had been a six-pound weight loss, and melena was present. When examined, she was cachectic and pale, and her liver was palpable 4 cm. below the right costal margin. Her hemoglobin was 3.8 gm. Preoperative bilirubin ranged as high as 32 mg. total, 18 mg. direct, and alkaline phosphatase was 82 King-Armstrong units. Fecal urobilinogen was 12 Ehrlich units per cent. Cholangiograms through the T tube demonstrated no patency of the biliary tree.

On June 29, after a series of transfusions had raised her hemoglobin to 13 grams, she underwent her fifth operation. The tumor had recurred locally and attained a size of 4 x 5 cm. It firmly surrounded the portal vein and the hepatic artery and had extended high into the liver hilum. After dissecting free the previous duodenal hepatic anastomosis, it became apparent that the total extrahepatic biliary duct system was obstructed with tumor mass. The left lobe of the liver was cut across, and a dilated intrahepatic biliary duct 1.5 cm. in diameter was identified. This was cannulated, and an operative cholangiogram demonstrated the dilated ducts in that lobe and confirmed the total duct obstruction at the hilum. The left lobe of the liver was then further incised until a duct 5 mm. in diameter was found, and a Roux-y hepatojejunostomy was performed. Postoperatively her course was very smooth, her bilirubin decreased to 12.3 mg. total, 5.7 mg. direct, and her alkaline phosphatase decreased to 58 King Armstrong units. At the time of this report she is four months postoperative, maintaining full household activities, is pain-free, and has gained four pounds. She has just begun a course of X-ray therapy to the liver area with hope of further palliation. Her hemoglobin has remained in the normal range and her bilirubin is at present 4.9 mg. total, 2.4 direct.

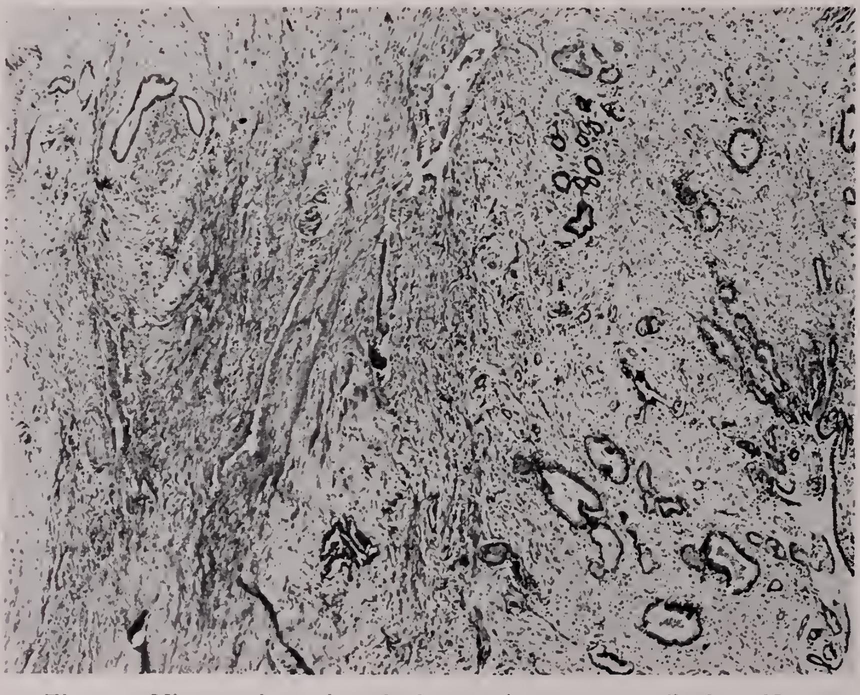

Fig. 1 — Microscopic section of adenocarcinoma of the bile duct. Note the well differentiated glandular structure. Also note the perineural infiltration in the upper left corner of the section. (Microscopic section times 40).

Discussion

Cancer of the extrahepatic biliary tree surprisingly accounts for about 6,000 deaths per year in the United States.[7] In various autopsy series it is reported to appear in 2.6 to 4.5 persons per thousand consecutive autopsies. Glenn has reported that three per cent of all cancer in the United States is in the extrahepatic biliary system.[1] In the Mayo Clinic series, the tumor is reported to be present in one of every 210 biliary duct operations.[6] The incidence is most prevalent in the fifth and sixth decades and does not seem to have a marked sex preference. Cases have been reported in the second decade of life.[3]

Symptoms

The initial symptoms of painless jaundice in this patient are quite typical. Symptoms of acute cholangitis do occur, but often, as in this case, only after surgical intervention. Pain does occur in about one-half recorded cases, though it often develops after the onset of jaundice. Marked weight loss frequently out of proportion to the degree or duration of associated symptoms is commonly present, though not exhibited in this case. The severe anemia present in this case is probably due to bleeding from the biliary tree as melena was present. Evidence of enteric bleeding, however, is frequently not present to explain the anemia seen in many cases of carcinoma of the biliary tree. Associated cholelithiasis is present in up to 40 per cent of cases.[10]

Pathology

Grossly, the tumor often appears, as in this case, in the form of diffuse scarred mass in a porta hepatis, though it may be papillary or nodular. Histologically, the tumor only infrequently appears as well differentiated glands, but most often is seen as papillary or undifferentiated adenocarcinoma.[8] The presence of well differentiated glands in juxtaposition to the biliary tree should immediately alert the surgeon to the possible presence of malignancy. Perineural involvement is pathogneumonic and every attempt should be made to demonstrate this finding.

Prognosis

The prognosis of cancer of the bile ducts is indeed very poor. The hope for prolonged survival lies in early diagnosis and radical surgery, especially in the differentiated type. Unfortunately, in the majority of cases the tumor is beyond resection for cure because of local extension into the porta hepatis and the liver parenchyma. Forty-five to seventy-five per cent have distant metastases at initial laparotomy despite a short history of preoperative symptoms.[2,9]

The first local excision with primary anastomosis was done by W. J. Mayo in 1903. Few local procedures such as this have been carried out, for in more than 74 per cent of the cases the tumor lies in such a position that no duct is available above the tumor for anastomosis.[6] A radical resection, described by Whipple in 1935 for tumors involving the duct more distally, has offered some hope in such cases. In a study of 172 cases, however, Sako reported the average survival was only 4.2 months.[8]

Continued

Treatment

The surgeon, therefore, must resort to palliative procedures in most instances. Tube drainage usually offers short term relief as exhibited by the several procedures attempted on the patient reported. The hepato-enterostomy which offered this patient her most comfortable existence was described in 1905 by Kehr and perfected by Longmire in 1954.[5] The use of this procedure allows enough bile product clearance to prevent itching and maintain fat breakdown for nutrition. Five of seven patients recently reported by Kulmeyer have met with similar success, but the long-term follow-up of these cases, as in ours, is not yet available.[4] Antacid should be given to the patients for prevention of the so-called Mann-Williamson type ulcer syndrome present with bile and pancreatic juice deviation from the stomach.

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By all means take a private room in the hospital, out of consideration for the friends who will come to tell you what's wrong with them. — Changing Times

A woman is as old as she looks to the man who likes to look at her. — Finley Dunne

Neurological Conference

Multiple Sclerosis*

Dr. Robert Soll**

The conference today concerns a patient with multiple sclerosis. This is a crippling disease which has its onset relatively early in life, often at the beginning of a person's productive career. The very name, multiple sclerosis, is one that carries an ominous forboding for many people because of the relentless exacerbations that usually follow a transient improvement, leaving the patient in even greater frustration and disability than before. The disease begins insidiously, often with a minor episode of limited paralysis or paresthesia of an extremity, or a visual disturbance. Frequently, after a comparatively short time, the patient begins to develop a weakness and stiffness of the lower extremities; or he may complain of a heaviness or numbness of his legs. He may note an increased urgency to urinate, and on occasion, he may be actually incontinent. Subsequently there may be a variable period of time, perhaps months, when the patient finds himself apparently in perfect health before again noting the reappearance of an unsteadiness in gait, due not only to weakness but also to imbalance. He may note a trembling of his hands, particularly on intentional movements. His speech may develop a slurred quality when long words are spoken. There may be slight choking on attempting to swallow liquids. The hands and feet may continue to "feel," but there is present a peculiar quality of numbness which the patient often has difficulty in describing. As the disease progresses, the patient finds that he is unable to continue gainful employment; medical costs mount, with resulting problems in maintaining his living conditions.

I'd like to call upon Dr. Olson at this point to give a brief historical account of this patient's illness.

Dr. Byron Olson***

The patient is a 43-year-old single, unemployed clerical worker with symptoms resulting from her demyelinating disease extending over the

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past four years. A few months prior to the onset of her illness, she had a period of severe chest pains, a pleurodynia-like syndrome for which she did not see a doctor. The first symptoms relating to her disease were numbness in her right arm and leg and an associated feeling of awkwardness during September 1960. This condition gradually improved over one month's time. Three months later, in December 1960, she developed decreased vision in her right eye. The only objective neurological finding at that time was temporal pallor of the right optic disc. Intramuscular ACTH therapy was given and was followed by some improvement. Her visual complaints subsequently continued with varying degrees of severity during the following year and a half.

In May 1962, she was hospitalized for severe impairment of vision in the left eye which did not respond to ACTH therapy. Later that year, she participated for six months in a secretarial course at the Sister Kenny Institute. Unfortunately, her typing improved only very slowly, due to mild inco-ordination. The working diagnosis at that time was demyelinating disease of unknown cause with some degree of psychogenic overlay. In December 1963, three years after the onset of her first symptoms, she was admitted to University Hospitals following a one-week history of numbness and awkwardness in the left arm and leg, plus blurred vision in the right eye. Physical examination revealed unsustained ankle clonus bilaterally and temporal pallor in both optic discs. Her gait was somewhat unsteady at that time. A ten-day course of intravenous ACTH therapy produced moderate subjective improvement. She was followed in the outpatient clinic over the subsequent nine months until early September 1964.

Of particular interest were her complaints of persistent daily nausea and vomiting during the early morning hours, only partially relieved by compazine or tigan. Intramuscular ACTH and a short course of Vitamin B_{12} were given regularly by a visiting public health nurse. The patient was again admitted to the University of Minnesota Hospitals on September 8, 1964, from the emergency room, after one week of increasing ataxia, vertigo, blurred vision and right-sided numbness, and after falling four to five times on the previous day. She slowly improved with intravenous ACTH therapy and was discharged to a nursing home, walking with some difficulty unassisted.

Her past history was unremarkable except for a 15-year history of occasional severe left-sided headaches which promote nausea and vomiting unless Empirin #3 tablets are taken promptly at the onset.

Physical examination during her recent hospitalization was unremarkable except for the neurological findings. She was a moderately well developed, thin, white female, prematurely gray, and variably co-operative. Her optic discs revealed marked temporal pallor bilaterally. The deep tendon reflexes were hyperactive in the lower extremities and there were positive toe signs bilaterally. There was decreased co-ordination and some tremor, both more marked in the right arm and leg. Subjective sensory signs were of questionable validity.

Dr. Soll

We have two particular problems with such patients: Financially they find it very difficult to continue private medical care because they are unable to maintain employment. Psychologically they need the consistent, empathetic care which their own private physician can offer them. Secondly, there is the problem of medical treatment itself. I would like to discuss the treatment that has gained the greatest acceptance up to the present. To begin our discussion I would like to ask Dr. Brantner about his psychological evaluation of the patient and her attitude toward her illness.

Dr. John Brantner*

The patient could be described as unco-operative as far as testing was concerned. I felt that any immediate administration of standard tests was going to yield completely unreliable results. The Peabody wide-range vocabulary test is used to evaluate severely handicapped people. The patient has an IQ of about 125, college-level intelligence. Brain damage tests were negative. There was no sign of central nervous system involvement. She does not show deterioration of thinking. A multiphasic test taken a month previously, showed depression, anxiety, discouragement, unhappiness, social withdrawal, and introversion. I spent much of the interview time chatting with her, attempting to get a better idea as to what kind of a person she was. She dresses well and appears considerably younger than her age. She was a likable individual and a very interesting one: intelligent and charming; but she quite rapidly erects a barrier between herself and other people. It is as though she is saying quite directly, "You are well and I am not. You have a future to look forward to; I do not. My plans have come to nothing; I am not able to be a secretary. Although I have been interested in art much of my life, I cannot draw. I cannot walk. All of my plans have come to nothing; therefore, there is no point in my going to see a doctor, for the doctors can do nothing." She resents the normal pleasantries in which one might indulge, and becomes somewhat angry at other people, saying in effect, "You can laugh; I have nothing to laugh about." At one time in her life, she wanted to be a commercial artist, but she is no longer much interested. As we were talking about other things, she drew a couple of lines and instantly made a fairly impressive sketch.

I can say with confidence that she is very intelligent, that she doesn't show psychological signs at all of central nervous system involvement or deterioration as a result of her disease, but that she is depressed, discouraged, unhappy, and unwilling to do anything about it at the present time. I was surprised to note that the disease was so relatively recent. Her attitude may, therefore, represent a more basic personality characteristic than a reaction to her disease.

Miss Helen Kretchmer**

At the time of the original referral the patient was having difficulty in walking and with balance. Her mother assisted her in maintaining her small apartment and probably did her cooking. The patient's father was an 8th grade graduate and worked as a machinist. He was ill with a heart condition in 1944, became very confused, and was cared for in a nursing home, and at home. The family was never on relief, due to the efforts of the children in contributing to the family finances and to the mother's working.

The patient had been a premature baby. Her mother had considered her frail from birth although she was not slow in developing. Both the patient's

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mother and the patient herself had the idea that she was a very weak person. This has seemed to influence the mother's treatment of her. The mother appeared to feel guilty about the patient's developing a demyelinating disease. I think this agrees with what Dr. Brantner has suggested — that possibly her discouraged attitude developed at a much earlier age and is not due to her present condition.

The patient graduated from high school and did well, although she was often out of school with illness. She was especially good in art and attended the Art Institute where she took drafting. She used her drafting experience at the Northern Ordnance during the war. She also did office work for different insurance companies. She changed jobs frequently. She was always somewhat withdrawn and found it difficult to be close to people. Nevertheless, her mother states that she had many friends and went out a great deal prior to development of her illness. After that time her personality changed; she did not want her friends to see her, and she felt that people would not want to associate with her.

At the present time she depends on her mother for personal assistance but does not wish to live in the same home with her. She had previously moved to within one block of her mother so that she could have more help. She would probably be best satisfied living in an apartment next door to her mother, so that she could retain independence. She does not have the money to pay for a private doctor, although I think she would be very well-suited to having a private doctor, as she does need continuity in care. The mother will remain a strong factor in her plans. In a guarded way, the patient has recently expressed great dissatisfaction with the nursing home in which she has been placed, but actually she now seems to be doing better physically. It is quite possible that she may be helped to lead a more normal life in a semiprotected boarding home placement near her mother. As far as her returning to work is concerned, I don't think that she would be able to hold a job.

Mrs. Shimamoto*

I would like to tell about the apartment in which she lived, where she was listed under an assumed name. She liked this apartment; in fact, she didn't want to move. When she applied for relief to pay the rent, the stipulation was that the landlord also was to make application to relief for payment. I am not familiar with the procedures, but he did not do so, and finally she was evicted. Her apartment was on the third floor facing the auditorium construction, where drilling started at 5:30 in the morning and continued until 11:00 at night. This was all she talked about when I visited at 8:00 a.m. She was quite unhappy and wanted to move near to her mother who was coming every day to help her.

Dr. Richard Foreman**

The patient said she went to her mother's to eat, but actually the mother went to the patient's apartment to prepare the meals. The patient stated that her mother could give her considerable help; but the mother really can't be expected to give her daughter much nursing care.

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Dr. Soll

The patient has been very independent most of her life. When she can't be independent, she is embarrassed. She has always paid her bills herself; now she can't pay them because she can't work. I think this is an extremely important aspect of this case. Is she a person who outwardly wants to appear independent, but actually has a great emotional as well as physical dependency on others?

Dr. Brantner

She does tend to reject people. Living alone is very important to her, but she recognizes that she can not possibly be an independent person, and this of course contributes to her condition.

Dr. Richard Magraw*

An illness of this type can put many things in different perspective. A person may continue through life with expectations that tomorrow he will start 'cashing in' on the good things of life, so to speak; then, if he has a heart attack, multiple sclerosis, or some other disabling disease, he will really be caught short in reaching fulfillment. This type of experience is an almost universal one in life and usually goes by the name of involutional reaction. I am not saying that this is what our patient has, but I think there are other illnesses with this same type of emotional reaction which she seems to have.

At this point in the conference, the patient was brought into the room for questioning.

Dr. Soll

(To the patient) I'd like to ask you what you feel are the prospects of your going back to work?

Patient

I don't think I could do it. I might be able to do a part-time job if it were very easy, otherwise I couldn't. I have nausea when I get up in the morning; it usually lasts most of the day unless I take something.

Dr. Soll: Are you getting around fairly well now, as far as walking is concerned?

Patient: Yes, I can walk pretty good. I have to watch so that I don't fall. I can't walk very fast.

Dr. Soll: Is your walking better than it was when you came into the hospital?

Patient: Yes, when I came in I was staggering so. I walked in but I don't think I could have walked out. I had poor co-ordination. I couldn't make my hands wash a dish and put it down. It seems simple but I couldn't make my hands do this.

Dr. Soll: What have doctors told you in the past as to what to expect from this condition?

Patient: Not a thing.

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Dr. Soll: They haven't told you anything about understanding your illness?

Patient: Not that I can remember, no.

Dr. Soll: What do you think of your condition?

Patient: I think eventually I am going to be much worse off than I am now. I am not looking forward to it.

Dr. Soll: Would you hold your hands out for us? Is the sensation in your hands different from what it used to be?

Patient: One hand does feel different. It seems weaker —

Dr. Brantner: Are you still in the nursing home?

Patient: Yes.

Dr. Brantner: How do you pass the time?

Patient: Sleeping.

Dr. Soll: Do you read or watch TV?

Patient: The TV doesn't look very good. The picture isn't good, and I don't think it is ever going to be because of my left eye. Things aren't perfect in the other eye either. My glasses can't be changed because I can't see the biggest letters anymore, so the picture on the TV doesn't look very good. I am not very happy. I want to be by myself.

Dr. Brantner

Would you prefer not being by yourself?

Patient

I prefer living alone. My mother lives only a block away and I can eat there every day. As far as that goes, she gets both our groceries delivered by the same grocery store. My mother usually has so many grandchildren to visit her that I can go over there to amuse myself. I used to like to go dancing, but I haven't been able to dance for about two years.

Dr. Brantner

Have you done anything about taking up painting again?

Patient

No, I can't do it. My sight isn't too good, and I can't tell the colors. I tried this a long time ago. I even quit work for six weeks to go to art school. You have to have quite a good education. An awful lot of people are interested in art, and it is hard to get into. I couldn't work and go to school. How would I pay for it? That's the problem. I could do a certain amount of sketching, but it wouldn't be as good as it was. I'd like to go to night school because there are all kinds of people from different walks of life.

There being no further questions, the patient was escorted from the room.

Dr. Foreman

I think I am the only one here who has had any personal contact with the patient in the ward situation during her hospitalization. We were not surprised that Dr. Brantner found her intelligence quite high. She is a very bright person, but it was also perfectly obvious to us that she did have organic involvement of the nervous system. She erects a wall between herself and the physicians. When visiting her during ward rounds, one could never converse with her, because she would lie in bed and wouldn't answer. If she did answer, frequently it was to make a hostile remark. On the other hand, it became apparent that she could do much more for herself than one would expect. She was seen by members of the staff to walk perfectly well with only a mild disability, whereas in objective testings she would stagger against walls, almost falling down. She probably had the actual capacity to do more than she did. The other thing was her extreme desire for independence. She definitely was not going to go anyplace but home, to a third floor apartment, in spite of the fact that when we met with her superficially, she could hardly feed herself or go to the bathroom unassisted. We did feel she could get along at a boarding home, and I am glad to hear that this suggestion has been made. She walked much better while in her room than she did at any other time in the hospital. So I think she gets along quite well physically.

Dr. Soll

It was apparent to me while checking her reflexes that the upper extremities were considerably less hyperactive than the lower. This finding is common in multiple sclerosis and demonstrates a correlation between the pathological process of the disease and the clinical picture. We have here a disease in which there is a multitude of lesions at random throughout the whole nervous system. The fact that her upper extremities are considerably less involved than her lower extremities is simply because there is less distance between the arms and the brain than there is between the legs and the brain; in other words, there are quantitatively more lesions within the whole spinal cord than in part of it. Thus a totally greater number of fibers to the leg are interrupted than to the arm. This is primarily the reason why multiple sclerosis patients have a much greater involvement in the lower extremities than in the upper.

Etiology

Attempts have been made to solve the dilemma of etiology, and thus unlock the key to its logical treatment. The possibility of an infectious cause has been repeatedly suspected, particularly by specific infecting agents such as viruses, bacteria, or even spirochetes. At no time has any evidence approaching conclusive proof been offered that an infectious agent was directly responsible. Faulty mineral metabolism, injury, heavy metal poisoning, alterations in the coagulability of the blood, and diet have also been suggested as possible factors. Heredity certainly may play a role; however, its significance cannot be denied in a great many diseases. Finally, an immunological relationship has been suggested, and here the evidence, although circumstantial, is impressive. We know that nervous tissue is potentially antigenic. Experimentally, central nervous tissue can incite an encephalomyelitis even when it is derived from the same animal. In addition, one can produce an exacerbating and remitting disease in guinea pigs using central nervous tissue as the antigen. The course is not unlike that of multiple sclerosis which we observe clinically. Experimental allergic encephalomyelitis has been closely allied etiologically with the immune mechanism. A significant percentage of multiple sclerosis patients have been found to have antibrain antibodies in their serum, far in excess of other neurological conditions in which central nervous system damage

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is also present. Pathologically, a similar perivascular cuffing of mononuclear cells is found within areas of the central nervous system, correlating with the demyelination in multiple sclerosis as well as in the experimentally produced encephalomyelitis.

Treatment

The use of ACTH in multiple sclerosis is the only method of treatment which has continued to be used over the past decade without dropping into disrepute. Since steroid therapy is well known for its use in allergic inflammatory conditions, the probability that its anti-inflammatory action contributes to the improvement of multiple sclerosis patients is great.

Assuming that multiple sclerosis is an autoimmune disease, it becomes exceedingly important to emphasize that an exacerbation of multiple sclerosis is as much a medical emergency as an acute attack of rheumatic fever or lupus erythematosus. The inflammatory reaction, found within the brain and spinal cord of acute multiple sclerosis, is causing damage, and the more quickly this is aborted, the less will be the functional deterioration of the patient. It is common that recovery following an exacerbation of multiple sclerosis leaves the patient less functional than before the attack. Therefore, rapid institution of therapy at the first sign of deterioration in a patient's condition is necessary. A doctor should instruct multiple sclerosis patients not to hesitate to inform him of any change in their condition that could imply another attack, regardless of how subtle the changes might be.

Our standard method of therapy at the University of Minnesota is to administer ACTH, either 40 or 60 units in 1000 ml. or 5% D/W over an eight-hour period for ten consecutive days. Histamine may be added to the intraveonus solution if desired at dosage of 2.75 mg./1000 ml. The patient is placed on a low-salt diet and an anticholinergic agent is used to decrease the possibility of gastric hyperacidity. Empirically the diet is supplemented by a high intake of vitamin B complex and C. Following the 10-day course of ACTH, steroid therapy may be tapered off, using decreasing increments of ACTH gel over the next 10 days; however, this is optional. Although side effects from ACTH therapy are not frequent, those that do occur are euphoria, psychoses, acne, edema, and GI bleeding. Usually side effects result during prolonged administration of ACTH. I would like to mention, finally, the common occurrence of rapid deterioration in a patient's condition during a febrile intercurrent infection. These infections should be treated promptly with appropriate antibiotic therapy. Here again, it is the duty of the physician to instruct the patient accordingly.

Dr. Magraw

About a year ago, Dr. George Thorn reported the idea of administering large doses of steroid every other day to avoid dampening the pituitary ACTH production.

Dr. Foreman

We haven't done studies on steroid excretion in patients receiving ACTH therapy. On the other hand we treat a great deal of multiple sclerosis using the schedule that Dr. Soll has outlined. To my knowledge no instances of withdrawal symptoms or symptoms of hypopituitarism have occurred after this type of regimen. Only rarely do we administer ACTH intramuscularly, following this 10-day course of intravenous therapy.

Dr. Soll

Some clinicians keep patients on ACTH for a considerable period of time. I do not believe, however, that prolonged administration is necessary. Once the acute process subsides, one can withdraw ACTH. A spontaneous clinical remission that would have occurred eventually is simply hastened by the ACTH; therefore, it wouldn't be necessary to continue prolonged use of the drug. Physiologically, I think this is better for the patient, so that he doesn't become completely dependent on ACTH. Of course it would again be instituted upon the next exacerbation of the disease.

Dr. Magraw

Do you think that anyone who gets multiple sclerosis proceeds inexorably downhill? Let me explain the background of my question. I've seen a number of people during my medical career who have very good findings for multiple sclerosis, two of whom have shown no progression during the past 20 years. I wonder whether you feel that there are more forms of this disease or is it sometimes just called by another name?

Dr. Soll

I think that multiple sclerosis has a wide spectrum of clinical forms. On the one hand there is postinfectious encephalomyelitis in which there is usually just one devastating attack. Then there are all degrees of multiple sclerosis, both acute, severe types as well as chronic, slowly progressive types. Finally, a condition such as Guillain-Barre syndrome may be on the other end of the scale, in which recovery usually occurs.

Dr. Foreman

It is possible that many patients at some time in their life may have pathological changes which would be indistinguishable from multiple sclerosis, symptoms of the illness occurring only once and never recurring? Possibly the percentage of these patients is much more common than the type of patients that have been diagnosed as having multiple sclerosis.

Vertigo in a teenager, or a transient episode of numbness or weakness in an extremity, which subsequently clears, are examples. Until we find a way of diagnosing multiple sclerosis absolutely, that is, finding the etiology and conducting appropriate laboratory tests, we have to make the diagnosis on clinical grounds. A good example is the clinical diagnosis of polio; there is a very set clinical syndrome which constitutes polio. When the cause of polio was discovered, the clinical syndromes included under the diagnosis of polio broadened tremendously and many disorders that would not previously have been called polio, came to be recognized as polio. Now multiple sclerosis may be much the same kind of thing.

Dr. Magraw

Dr. Kress, who is in private medical practice in Montana, is visiting us

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at the University Medical Center. I would like to ask him what perspectives he has on multiple sclerosis from his practice of internal medicine?

Dr. Jackson Kress*

As doctors, we like to feel we are doing some good. If we can't, we have a feeling of inadequacy. I think a similar example is the treatment of a cancer patient. When I was younger, I didn't know what to do about it, but now that I am older, one thing I know that I can do is give a patient some kind of support. I think it takes many years to acquire this ability.

Dr. Richard Foreman

Of course as neurologists, we are faced with a great many disorders in which there is no specific cure; so we are much more aware of the necessity of finding other ways to help the patient in the form of support, social planning, and the providing of special equipment to help him function better with his disability. It is really a joy to help a multiple sclerosis patient in these ways. You know you can't do anything specific to reverse the disease process, but there is a tremendous amount of support these people need and can have if the physician focuses on this aspect of the problem. Such patients can be managed for many years in the home situation, if they receive sympathetic care.

Dr. Brantner

This is a patient whose problems are not entirely and solely medical, but of a social nature as well. She also has serious economic problems: living, for instance, on $1104 per year. In addition, she has personality problems which probably existed before but were not brought to anybody's attention. Now the attack on these personality problems might be more validly approached than before she became so disabled.

Robert Soll, M.D.
Neurologist
University of Minnesota
Medical Center

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*Clinical assistant professor, Missoula, Montana.

Participating in the conference of Oct. 15, 1964 are Mrs. Shimamoto, Public Health Nurse from Minneapolis Health Departmet Visiting Nurse Service and Dr. Jackson E. Kress, Clinical Assistant Professor, Missoula, Montana. The following participants are from the University of Minnesota Medical Center: Dr. Richard Foreman, Chief Resident of Neurology and Medical Fellow Specialist; Dr. Richard Magraw, Director, Comprehensive Clinic Program; Dr. John Brantner, Clinical Psychologist; Miss Helen Kretchmer, Supervisor and Assistant Professor of Social Service; Byron Olson, Senior Student Doctor; and Dr. Robert Soll, Neurologist and Chairman, Adult Community Services.

We usually meet all of our relatives only at funerals where somebody always observes: "Too bad we can't get together more often." — Sam Levenson

We do not cease playing because we are old; we grow old because we cease playing.
— Joseph Lee

Infections of the Urinary Tract

Part II — Some Microbiologic Considerations*

WILLIAM J. MARTIN, M.D.**
RICHARD D. WAGONER, M.D.**
Rochester, Minnesota

Collection of Specimen

Attempts should be made to secure information about the patient's urinary status with the least amount of manipulation of or disturbance to the urinary tract. Catheterization is not necessary as a routine procedure in the microbiologic study of the urine in males; examination of a second-glass specimen is sufficient. In men, the head of the penis is cleaned with cotton that has been moistened with warm water. The patient passes the first part of the specimen into one container, the remainder into a second container or sterile bottle. The first container, which may contain urethral and prostatic secretions and a certain amount of vesical detritus, is discarded. The specimen for microbiologic examination is taken from the second.

In women, although specimens obtained by catheterization continue to be preferred by some urologists, considerable data indicate that in women, too, specimens obtained by the clean-voided technic often may suffice; this avoids obvious physical, psychologic, and infectious hazards.[11-18] In women, the patient or a nurse separates the labia with one hand and with the other wipes the urethral orifice with a pledget of moist cotton. A woman, unable to produce a second-glass specimen while in the lithotomy position, may straddle a low stool on which two basins are placed side by side. She voids into one basin and then into the other. The specimen is taken from the second basin or is caught directly in a sterile bottle. If the bedridden woman is unable to void in the lithotomy position, she can use a commode, or the collection can be made in a container held beneath a regular toilet seat. In some institutions, the vulva, prior to collection of the specimen, is cleansed with two applications of green soap and water, followed by two rinses with sterile distilled water. Also, cleansing of the vulvar region with hexachlorophene has been recommended. Culture of urine obtained from females by the clean-voided technic appears to give false-positive results in less than 15 per cent of specimens.

Percutaneous suprapubic aspiration of the bladder in order to collect urine for culture is rather heroic as a routine procedure.

Immediate Examination or Refrigeration of Specimen

Urine specimens should be studied for bacterial numbers within one hour after passage, or else the sample should be refrigerated, since storage at room temperature permits bacteria to increase significantly and the bacterial count easily may reach 10,000,000 per milliliter in 18 to 24 hours. However, urine that has been kept under constant refrigeration for longer than 24 hours should be discarded, since saprophytic bacteria multiply and cellular elements may dissolve.

Quantitative Cultures

The presence of 100,000 or more bacteria, cultured from 1 ml. of urine, characterizes 95 per cent of specimens of urine passed by patients with urinary infection. Many clinical infections have bacterial counts of 1,000,000 to 10,000,000 organisms per milliliter. Counts of less than 10,000 bacteria per milliliter usually are not significant. It is wise

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*See Part I, Minnesota Med., January issue, Page 95.
**Section of Medicine, Mayo Clinic and Mayo Foundation.

to request two quantitative counts of different specimens, if possible, before giving a definite opinion regarding the existence of urinary infection solely on this basis.

Many investigators today believe that, since quantitative culture of the urine appears to be at least 95 per cent reliable, and since the microbiologic correlation between specimens obtained by catheterization and by clean voiding exceeds 85 per cent, catheterization for microbiologic diagnosis also is unnecessary in women patients.

In attempts to quantify bacterial number, liquid culture media such as broth are not used; cultures are made from various dilutions of urine on pour-plates of solid agar, after which the colonies can be counted. In some institutions a streak-plate technic is used. Use of standard volume-calibrated loops for inoculation of the cultures appears to assure more reliable quantitation. One method consists of employing 0.1 ml. of urine, diluted 1:100 and 1:10,000 with sterile isotonic saline, which is then cultured; in addition a loopful of undiluted urine is inoculated into a medium such as thioglycollate for anerobic organisms. A loop with an inside diameter of 1.45 mm. and designed to deliver 0.001 ml. of urine and a loop with a diameter of 4 mm. and designed to deliver 0.01 ml. of urine also have been recommended.

Low counts may be misleading in infections due to organisms which tend to form swarms, clusters or chains, since there is a propensity to form a single colony. Special media may counteract the swarming tendency of protei, but clusters of staphylococci and chains of streptococci may pose difficulty. Misleading low counts also may be encountered with slow-growing organisms such as bacteroides.

Bacteriuria on Direct Examination

Bacteriuria is detected in a considerable number of patients who otherwise appear to have a normal urinary tract; that is, they lack pyuria and urinary symptoms. The simplest way to detect bacteriuria, asymptomatic or otherwise, is to examine an uncentrifuged specimen of urine that is stained by the gram method or by methylene blue. If bacteria are found, the count is taken to be more than 100,000 per milliliter. The intrinsic error in this procedure is said to be less than 20 per cent; the procedure often provides pertinent data prior to quantitative urine culture reports but preferably should be corroborated by them.

In overt urinary infection, examination of a stained specimen of urine allows classification of bacteria found therein into the broad groups of gram-positive and gram-negative organisms. If antimicrobial therapy is initiated on this basis, the patient may be on his way to recovery by the time the results of culture and other microbiologic studies are reported.

Chemodetection of Bacteriuria

Use of such agents as triphenyltetrazolium chloride to detect significant bacteriuria is reported to correlate with microbiologic procedures in more than 80 per cent of cases. The urine to which the chemical agent is added is incubated, and the colored precipitate that is formed by the reduction of the agent by bacterial metabolites indicates significant bacteriuria (100,000 or more organisms per milliliter). In this reaction, the metabolizing bacteria reduce the colorless triphenyltetrazolium chloride to pink or red insoluble triphenylformazan. A similar colorimetric procedure is referred to as the Greiss technic. Positive results with these tests should be confirmed by cultures.

Presence or Absence of Bacteriuria

While bacteriuria on direct or other examination does not, ipso facto, indicate pyelonephritis, the more persistent the bacteriuria, the more likely that pyelonephritis is present. Bacteria isolated from the urinary tract may represent, in addition to urinary infection, (1) histologically deranged kidneys, that is, second invaders, (2) normal urethral organisms, and (3) contaminants.

Failure to find large numbers of bacteria in the urine of a patient with a classic syndrome of urinary infection should raise the question of (1) precultural administration of antibacterial agents, (2) ureteral obstruction, (3) excessive hydration, which may be indicated by low specific gravity of the urine,

(4) a urinary pH of less than 5 which, per se, can produce bacteriostasis, or (5) slow-growing bacteria, such as anaerobic bacteroides organisms, which may require as much as three weeks before cultures reveal growth.

A single negative test for bacteriuria, whatever method is used, does not exclude infection, since organisms may be spilled into the urine only intermittently.

Pathogens

Gram-negative bacteria usually are associated with acute infections, and gram-positive bacteria may be isolated in certain chronic infections. Over-all, however, infection is more commonly due to gram-negative bacilli; of these, Escherichia coli has been most frequent. E. coli, Aerobacter, and Proteus organisms probably account for more than three fourths of all urinary infections. In recent years there may have been a decline in the incidence of infection due to E. coli and a corresponding rise in those due to Klebsiella-Aerobacter, and Proteus organisms. Pseudomonas organisms are most commonly responsible in patients who have urinary instrumentation including indwelling catheterization and in those who have been receiving antibacterial therapy. Other gram-negative bacilli that are infrequently causative include strains of Achromobacter species and organisms belonging to the Mimae group and genus Serratia. Of the gram-positive organisms, Staphylococcus aureus and streptococci, usually Str. faecalis, predominate but in recent years, infections due to these organisms appear to be of decreasing incidence. In a few infections, usually of the acute variety, culture of the blood also is positive.

Epidemiologic studies suggest that some strains of the Enterobacteriacea are associated with infections of the urinary tract more commonly than other strains. Escherichia serotypes 0-1, 0-2, 0-4, 0-6, 0-75, and 0-117 probably are responsible for almost half of the infections due to E. coli. Escherichia serotypes 0-4, 0-6, and 0-75 most likely cause infections in hospitalized patients. The serotype 0-1 may be the most common type responsible for infections in nonhospitalized patients. A high percentage of infections from Klebsiella-Aerobacter organisms are due to capsular types 8, 9, and 10. Of the four strains of Proteus species, Proteus mirabilis appears to be slightly more frequently encountered than vulgaris, while rettgeri and morgani are uncommon.

So-called urea splitters, which may require acidification of the urine for their eradication when certain regimens are employed, include Proteus, Klebsiella-Aerobacter, Pseudomonas, and certain staphylococcal organisms.

If nephrocalcinosis develops in patients with renal tuberculosis, brucellosis, or salmonellosis, secondary bacterial invaders may obscure the underlying process. A paradox in the pathogenesis of nephrocalcinosis is that among its several causes is infection; conversely some workers believe that it follows the use of sulfonamides.

One type of bacteria commonly disappears during treatment of the infection and is replaced by another; this phenomenon of "replacement of pathogens" occurs in about 25 per cent of cases. Infections due to multiple organisms are present in about 10 per cent of cases and usually are indicative of (1) urinary manipulation including catheterization, (2) recent antibacterial therapy, or (3) a complicated or chronic process.

Especially when so-called bacteriostatic or suppressive drugs are used, negative follow-up cultures of the urine should not cause relaxation of scrutiny, since the infection may recur shortly. In the laboratory, with concentrations of drugs unattainable in the body, agents may produce irreversible destruction of bacterial viability or, in other words, a "killing effect" on bacteria. However, the term "bactericidal" is employed to designate drugs that may do so in vivo, that is, drugs that produce a killing effect on bacteria when administered in concentrations that can be tolerated by the host. The bactericidal agents include the penicillins, streptomycin, bacitracin, neomycin, kanamycin, polymyxin B, colistin, ristocetin, cephalothin, and vancomycin. "Bacteriostatic" agents are those whose concentrations in the body are insufficient to kill bacteria; that is, they produce a reversible inhibition of bac-

Continued

terial proliferation. Bacteriostatic agents may be ineffective when used alone, except in acute uncomplicated situations. These agents include the tetracyclines, chloramphenical, erythromycin, novobiocin, triacetyloleandomycin, the sulfonamides, nitrofurantoin, the acidifying agents, methenamine mandelate, and nalidixic acid.

Although the terms "bactericidal" and "bacteriostatic" may not be ideal, there is a need to be familiar with the concept that they identify. Theoretically at least, optimal therapy with bacteriostatic agents probably requires continuous maintenance of adequate concentrations in the body, more so than does treatment with bactericidal drugs, since, after limited exposure to a bacteriostatic agent, bacterial growth is more likely to be resumed. Also, some agents that ordinarily are bactericidal may be only bacteriostatic when administered in less than optimal concentration.

"Sensitivity" Tests

The results of in-vitro bacterial susceptibility tests, while of great help in certain refractory infections and in those due to staphylococci, cannot be taken as dogma, since a bacteriostatic agent may seem to be indicated on this basis, but it may be known empirically that unless a bactericidal effect is obtained, treatment will be ineffective. In infections due to certain organisms, the pathogens invariably are sensitive to a given regimen; hemolytic streptococci remain susceptible to penicillin, enterococci to penicillin-streptomycin, and Pseudomonas organisms to polymyxin B. Experience also may indicate that certain antibacterial agents will be effective, despite bacterial susceptibility tests to the contrary. As an example, in treating some infections due to Proteus and Klebsiella-Aerobacter organisms, we have noticed that despite resistance of the organisms to tetracycline and streptomycin in the laboratory, eradication of the infection has coincided with the clinical use of these agents in many cases.

Empiric knowledge has accumulated sufficiently to indicate that bacterial susceptibility to antibacterial agents need not be determined routinely in acute nonstaphylococcal urinary infections, since they are time-consuming and expensive and may contribute no additional help. When an acute infection (regardless of bacterial etiology) is resistant to therapy in recurrent or chronic infections, susceptibility tests in conjunction with others (including urographic and cystoscopic studies) may prove rewarding. Bacterial susceptibility tests performed by the disk-plate or agar-diffusion method are not as reliable as those done by the tube-broth or cup-plate dilution method.

Pyuria

As aforementioned, pyuria and bacteriuria are not invariably associated. Significant bacteriuria may be present without pyuria, and the presence of pyuria does not necessarily indicate infection. If the presence of pyuria is relied on to indicate infection, the error may vary from 25 to 50 per cent; that is, in a substantial number of patients with pyuria there is no infection. In dehydration, after certain drugs have been used, in women with vaginitis and in men who have had transurethral prostatic resection (among other causes) pyuria is frequent but not reflective of urinary infection.

Clinicopathologic Correlation

Chronic urinary infections are found in about 10 per cent of routine necropsies and in 25 per cent of necropsies on previously hypertensive patients, but ante-mortem diagnosis of such infections is made in a lesser number of cases. At the present time, it is suspected that individuals with asymptomatic bacteriuria may account for this discrepancy among subjects found at necropsy to have unsuspected pyelonephritis. Since about 50 per cent of chronic infections are relatively asymptomatic, about 10 per cent of acute infections lack urinary symptoms, and significant bacteriuria may be present without causing pyuria, it is evident that a sizable percentage of infections may not cause urinary symptoms or abnormal findings on routine urinalysis. Consequently, it is good judgment to search for bacteria in stained specimens of urine from all patients, with or without pyuria or urinary symptoms, before deciding on their urinary status.

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Perkins Tractors

Toward the close of the eighteenth century, Elisha Perkins, an American physician, was curing disease right and left with two little, supposedly magnetic, pieces of metal called tractors. He did so well that even George Washington got a pair. After Elisha died, his son took the tractors to England, where he made a great stir and enlisted the support of the nobility. Unfortunately for him, the famous Dr. Haygarth was skeptical. First he held clinics at which he demonstrated how patients lost their pains when the affected parts were stroked with the tractors. Then, when everyone was much impressed, he took out his penknife and cut the supposed magnets in two; they were imitations made of wood. In the reaction that followed, educated England laughed, and Perkins left for home. (Walter C. Alvarez)*

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*Rapport, Samuel, and Wright, Helen: Great Adventures in Medicine. The Dial Press, New York, 1952, p. 12.

Byzantine Remedy for Colic

Remove the nipple-like projection from the caecum of a young pig, mix myrrh with it, wrap it in the skin of a wolf or dog, and instruct the patient to wear it as an amulet during the waning of the moon. Striking effects may be looked for from this remedy. (Alexander of Tralles, 525-605)*

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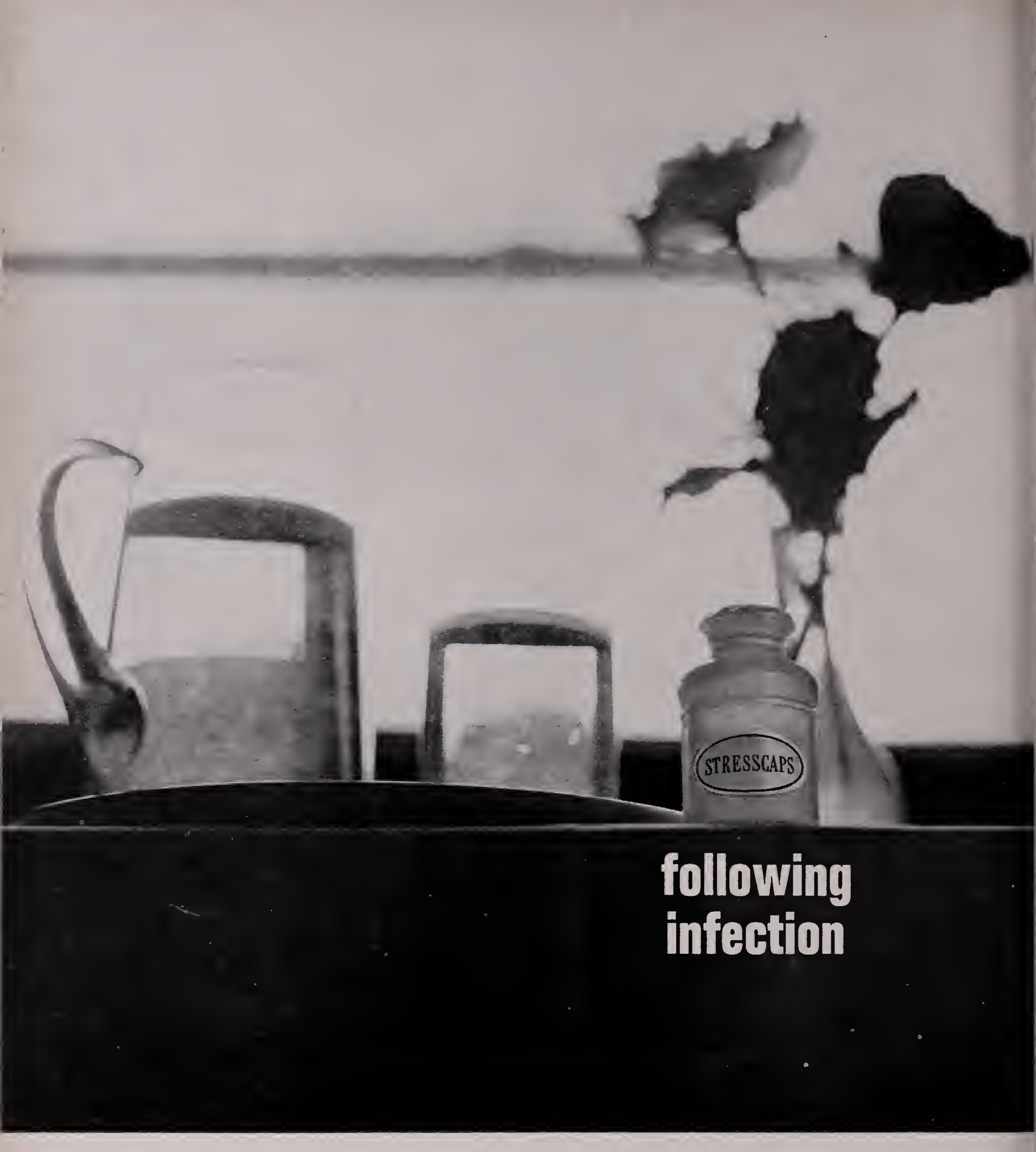
*Rapport, Samuel, and Wright, Helen: Great Adventures in Medicine. The Dial Press, New York, 1952, p. 44.

President's Letter Continued from Page 151.

citizens so that the voluntary approach may attract the widest support. In Minnesota we are fortunate to have Dr. Robert N. Barr as the secretary and executive officer of the State Board of Health because he has encouraged the voluntary approach. The understanding and support of the physicians of our state in sound hospital planning will be important factors in limiting the trend toward legislative control.

J M Stickney M.D.

J. M. Stickney, M.D.
President
Minnesota State Medical Association



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Grand Rounds

Pheochromocytoma—Pitfalls in Diagnosis*

Pheochromocytomas are tumors of the sympathetic nervous system which secrete excessive quantities of the catecholamines, adrenalin and noradrenalin into the blood stream.[8] About 90% originate from the adrenal medulla. Approximately 10% originate within the para-aortic bodies (organs of Zuckerkardl) and are termed paragangliomas.[23]

The first description of pheochromocytoma was made by Frankel in 1886. Paroxysmal symptoms were described by Labbe in 1922. The first successful removal was done by Mayo in 1927. In 1928 Pincoffs made the first preoperative diagnosis.[23]

Incidence

Pheochromocytoma may occur equally in both sexes. The youngest reported patient was a three-month-old baby. The peak incidence is between 20 and 50 years.

Occurrence

Miles reported that pheochromocytoma occurred in 1.3 per 100,000 admissions. Grace Hospital in Detroit, Michigan, reported an occurrence of 2.5 per 100,000 admissions.[32] Among hypertensives: Smithwick, 5 per 1,000 during sympathectomy; Graham, 5 per 1,000 during sympathectomy; Kvale, 6 per 1,000 hypertensive studies. Body Build: Almost always thin.[8]

Pathology

Ten per cent of the tumors are bilateral; if unilateral, the tumor usually occurs on the right side. Pheochromocytoma may be familial. Tisherman et al. described the occurrence of pheochromocytomas in several branches of a large family, frequent neurocutaneous disorders in other members, and an association of the tumors with metabolic cataracts and renal artery stenosis.[25] Calkins and Howard described the first familial occurrence of

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*Medical Grand Rounds, Mt. Sinai Hospital, October 13, 1964.

Continued

pheochromocytoma in 1947. Since then, 12 other affected kindreds have been identified for a total of 13 cases. About 20% of these tumors are multiple.

The tumors usually range from 1 to 10 centimeters in size, but several weighing up to 2,000 grams have been reported. They are usually encapsulated and are soft to firm in consistency, depending upon their size and the extent of degenerative change. The external surfaces are gray, whitish-yellow, or most often reddish-brown in color. All are well vascularized. They may metastasize to liver and bones, but histologically it is quite difficult to predict malignancy in the primary tumor.

Sites

90% in adrenal medulla; 10% — extra adrenal; a) Organ of Zuckerkardl — reported by Ortega in 1952. b) Pleural cavity — Philips, 1940. c) Hilum of the kidney — Von Euler et al., 1955. d) Urinary bladder — Zimmerman, 1953, — 13 cases reported.[30]

Clinical Types

There are many clinical types, but the simplest division is into two categories.

Persistent Hypertension

This group of patients have persistent rather than intermittent hypertension. In the Mayo Clinic series, two out of three were women. In this type paroxysmal attacks are common and blood pressure goes to much higher levels. Blood sugars were elevated in two thirds of the Mayo Clinic series and the basal metabolism rate was high in 90%.

Paroxysmal Hypertension

Peak age is from 30 to 50 years, with equal frequency in males and females. Attacks or spells may occur as often as every hour or as seldom as once in two or three months. They may last only 30 seconds or as long as one week. Headache is the most common symptom. Palpitation, perspiration, pallor, nervousness and tremor occur less often.

Symptomatology

The symptoms and findings during spells or attacks are variable. Hypertension (persistent or paroxysmal), headache, palpitation, perspiration, pallor, nervousness, tremor, vasomotor phenomena, elevated body temperature, gastrointestinal symptoms, weight loss, glucose intolerance, glycosuria and increased basal metabolism rate, all may occur or only a few may be present.

Diagnosis

The diagnosis of pheochromocytoma cannot be established on the basis of symptomatology alone, since many conditions such as cerebrovascular insufficiency, hyperventilation syndrome, paroxysmal tachycardia, migraine headache, hyperthyroidism, and anxiety states may be responsible for similar symptomatology.

Suspicious Symptoms

Pheochromocytoma should be looked for if one finds: 1. hypertension, paroxysmal or persistent; 2. hyperglycemia and glycosuria without ketosis; 3. hypermetabolism — tachycardia, excessive sweating, etc.; 4. recurrent bizarre spells.

One must correlate the above symptomatology with positive pharmacologic tests (Regitine, Histamine, Tyramine) and demonstration of elevated levels of metabolites or norepinephrine and epinephrine, such as vanillan mandelic acid and plasma and urinary catecholamines.

Suprarenal Mass

Further evidence for pheochromocytoma is the demonstration of a suprarenal mass by: 1. plain X-ray film, 2. excretory urogram, 3. excretory urogram tomography, 4. cystoscopic examination, 5. abdominal aortography, 6. presacral injection of CO_2.

Summary

The diagnosis of pheochromocytoma should be based on cumulative evidence from four features of the disease: 1. witnessing of a typical spell with documentation of associated hypertension; 2. presence of elevated values of catecholamines in the urine or plasma, or a positive vanillan mandelic acid (VMA) test, preferably after a hypertensive episode; 3. positive response to pharmacologic testing: "provocative" Histamine test in normotensives or "suppressive" Regitine test in hypertensives or during the hypertensive crisis, or a positive Tyramine provocative test; and 4. presence of metabolic effects of epinephrine; positive glucose tolerance test, hypermetabolism without hyperthyroidism.[11]

Electrocardiographic Changes

There are several electrocardiographic abnormalities which are found in pheochromocytoma:[35]

Abnormalities of rhythm, such as: 1. wandering pacemaker, 2. auricular tachycardia, 3. sinoauricular dissociation, 4. auricular premature contractions, 5. auricular flutter, 6. auricular fibrillation, 7. nodal tachycardia, 8. ventricular premature contraction, and 9. ventricular tachycardia.

Abnormalities of ischemia include: 1. low amplitude or inverted T-wave, 2. prominent P waves, and 3. characteristic diffuse distribution of T and ST wave changes.

Localization of Tumor

Once the diagnosis is established, an attempt should be made to localize the tumor by: 1. Palpation of abdominal quadrants. About 14% of cases are palpable.[6] 2. Intravenous pyelograms may show the tumor distorting the renal pelvis or displacing the kidney in 56% of unselected adult cases[6] and 31% of the cases in children.[5] 3. The tumor can sometimes be located by tomography, calcification being seen on the X-ray film or by the production of a hypertensive attack by massage in a particular body area.[5] 4. Presacral air injections and aortography are helpful but carry some risk. 5. When localization is particularly essential (e.g., following negative surgical abdominal exploration), a catheter may be inserted into the vena

Continued

cava and samples of blood obtained at different levels for catecholamine determination.[7]

Treatment

The treatment of choice is surgical removal of all tumor tissue. However, if the patient is a very poor surgical risk, drug therapy may be tried. Bellas treated a patient for eight years with Phentolamine Hydrochloride, 25 mg. every three hours during the waking hours.[20] Alpha Methyldopa, a decarboxylase inhibitor, will decrease norepinephrine production.[24] It may also be used to diminish sweating, flushes, palpitations and headache in unresectable pheochromocytoma.[29]

The efficacy of the prolonged administration of oral Phentolamine was first demonstrated by Iseri et al. and has been recently recommended as preoperative treatment for all patients with pheochromocytoma.[36]

Diagnostic Tests

Many drug tests have been suggested to differentiate between essential hypertension and pheochromocytoma. However, none are completely reliable. The tests also carry some danger, and fatal results have been reported. The following tests have been used.

Histamine Test

The first pharmacologic test was the Histamine test introduced by Roth and Kvale in 1945. This test is used when the basal blood pressure is less than 170/110. Five hundredths of a milligram of Histamine base in 0.5 ml. of normal saline solution is injected intravenously, after basal blood pressure is established. As a precautionary measure, Regitine should be ready for immediate administration if the blood pressure becomes alarmingly high. A cold pressor test should be done just prior to the Histamine test.

Blood pressure is determined every 30 seconds after the injection. Usually the blood pressure increases rapidly and is maximal in two minutes. The test is positive if the systolic pressure rises 20 mm. of Hg or more above the highest reading obtained with the cold-pressure test. This rise in blood pressure, usually accompanied by symptoms which characterize an attack, should occur within two minutes after the injection of Histamine, following an initial drop in blood pressure which occurs in the first 30 seconds after injecting Histamine. If the test is positive, one should inject 5 mg. of Regitine intravenously to abort the attack induced by the Histamine. This is also additional diagnostic evidence, if abortion of the attack occurs.

Phentolamine Test

If basal blood pressure is above 170/110, 5 mg. of Phentolamine (Regitine) is given intravenously. If blood pressure drops by at least 35 mm. of Hg in the first four or five minutes after injection and then returns to the basal level in 10 to 15 minutes, the test is positive. A decrease in the blood pressure in some apprehensive patients may occur during the first one to two minutes in the absence of a tumor; but the blood pressure returns to the basal level in one to two minutes.

Mecholyl Test

Mecholyl, like Histamine, stimulates the release of catecholamines from the tumor. The dose is 10 to 25 mg. subcutaneously. But it offers no advantage over the Histamine test and is more dangerous.

Dibenamine Test

Four hundred mg. in 500 ml. of 5% dextrose is injected intravenously over one to two-hour periods, producing a slowly developing but prolonged lowering of blood pressure. However, the test is neither specific nor reliable.[3]

Tetraethylammonium Test

This drug causes a release of catecholamines from the tumor and also blocks regulating mechanisms of secretion. It is seldom used.[4]

Benzo Dioxane Test

Fifteen to 20 mg. is given intravenously over a period of two to three minutes, during which the blood pressure is recorded at 30-second intervals for three minutes and then 60-second intervals for 15 minutes. A fall of 30 mm. within four minutes after the start of injection is a positive test. Dangerous pressor responses sometimes occur with or without a pheochromocytoma. False negative reactions are more common than with Regitine.[2]

Tyramine Test

Recently a new test has been reported: the tyramine test. An intravenous infusion of 5% dextrose is started in one arm, and blood pressures are determined in the other arm using a mercury manometer and inflatable cuff. Basal blood pressure is then established within 10 to 20 minutes. Before doses of Tyramine (500 μg to 2,000 μg) are given, it must be established that there is no response to the injection of a placebo(isotonic sodium chloride solution). The blood pressure is recorded every 30 seconds after injection until the systolic blood pressure returns to the base line. The blood pressure is again recorded for another 10 to 15 minutes, after which another injection is given. A positive test is a rise in systolic pressure of 40 mm. or more within two minutes and a return to base line within 12 minutes after injection. This test has few reactions; no disturbing symptoms are elicited; and it is easy to perform.[12]

Pitfalls Encountered in Various Diagnostic Tests

It is essential in the use of the pharmacological tests that a reliable basal blood pressure be obtained. This is often neglected.

False positive results may occur if sedatives or narcotics are taken within 48 hours of the test. Sedatives inhibit the blood-pressure rise during the cold pressor test, and increase in the blood pressure during the Histamine test may be greater than during the cold pressure test, suggesting the presence of a tumor. Sedatives and tranquilizers in patients with sustained hypertension may cause a fall in blood pressure typical of that produced in pheochromocytoma following intravenous Regitine. Uremia may cause a false positive Regitine test. Antihypertensive drugs should be withheld during the same period.

Hydralazine hydrochloride (Apresoline) and Reserpine should not be given for at least two weeks prior to testing, as these drugs produce false

Continued

negative results. Vasoconstrictive drugs used for nasal stuffiness may produce a profound fall in blood pressure for as long as 40 minutes after intravenous Regitine.

The disadvantages of catecholamines are: 1. they require services of skilled technicians and equipment of a type found in only the more elaborate research laboratories. 2. Meticulous attention must be paid to the patient's previous medicines. 3. Technique of preservation of urine samples is necessary. 4. Timing of collection of samples in those patients whose symptoms are paroxysmal in nature is required.[8]

Vanillan mandelic acid (VMA) is increased in shock, coma, metastatic malignancies, pulmonary insufficiency, or carcinoid tumor with metastasis.[21]

Increased catecholamines may be found 1. in patients who have received adrenergic products like Reserpine, Vitamin B_{12}, or barbiturates; 2. in patients who have eaten bananas or vanilla, and 3. in patients with anxiety or after strenuous physical exercise.[8]

Increased urinary vanillan mandelic acid (VMA) is found in patients with neuroblastomas, ganglioneuromas and ganglioneuroblastoma.[8]

Case Report

A 26-year-old married white woman was admitted to Mount Sinai Hospital, September 13, 1964, with chief complaints of headache and high blood pressure. She had had recurrent severe headaches for three years but no apparent hypertension. Three months before admission, elevated blood pressure (180/120) was discovered during a routine examination. Hypertension persisted during this three-month period. She denied any paroxysmal "spells," however, though her headaches were intermittent, coming on suddenly and lasting one to four hours. She had always been underweight and thin. Prior to admission she had been admitted to another hospital where a Regitine test was positive and an intravenous urogram and an aortogram revealed findings suggesting depression of the left kidney by a suprarenal mass. Urinary catecholamines were 29 mcg/24 hr. (normal: up to 103 mcg/24 hr.). She was admitted to Mount Sinai Hospital for surgical exploration.

Physical Examination

An examination on admission revealed a thin young woman complaining of headache. Blood pressure was 180 systolic and 124 diastolic in both arms. Peripheral arterial pulses, including femorals, were normal. The retinae showed arteriolar narrowing and A-V nicking. The aortic second heart sound was accentuated. No abdominal masses were felt. The remainder of the physical and neurological examination was negative.

Laboratory Studies

Hemoglobin, white blood count, sedimentation rate and urinalysis were normal. BUN was 19 mg%, CO_2 content 26 meq/1, chlorides 103 meq/1, sodium 141 meq/1, and potassium 4.6 meq/1. Prothrombin time was normal. Fasting blood sugar was 90 mg%. PSP dye excretion was normal. Urine culture was negative. Urinary 24-hour sodium and potassium were 154 and 90 meq, respectively. Urinary catecholamine excretion was 358 mcg/24 hr. (Normal: up to 103 mcg/24 hr.) Chest X ray showed minimal left ventricular enlargement. An electrocardiogram showed S-T-T wave changes consistent with left ventricular hypertrophy.

Hospital Course

The patient's blood pressure fluctuated in the range of 140/84 to 210/130 following admission. A Regitine test was done beginning with a basal pressure of 184/118. Within one minute after intravenous injection of 5 mg. Regitine, the blood pressure fell to 138/80 and then gradually rose over 10 minutes to 164/110.

On September 18, 1964, an abdominal exploratory operation was performed. The kidneys appeared normal and no adrenal mass was present. The upper and lower abdomen was explored by palpation and no abnormality found. A renal biopsy was taken and the abdomen closed. Histologic examination of the removed renal tissue revealed moderate arteriolar nephrosclerosis.

The patient made an uneventful recovery from surgery and was discharged from the hospital to be managed as an outpatient with antihypertensive drug therapy.

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13-36 can be obtained from Grand Rounds Editor at Mt. Sinai Hospital.

E. R. Bravo, M.D.
Mt. Sinai Hospital

No Words Wasted

Babbling women were the bane of Abernethy's* life. He would interrupt them by ordering them to open their mouths, then tell them 'Now shut your mouth and keep it shut.' One tale is of a lady who called on him with a cut finger. The dialogue went:

First day: Abernethy: Cut?
Patient: Bite.
Abernethy: Dog?
Patient: Parrot.
Abernethy: Go home and poultice it.
Second day: Abernethy: Better?
Patient: Worse.
Abernethy: Go home and poultice it again.
Third day: Abernethy: Better?
Patient: Well.
Abernethy: You are the most sensible woman I ever met. Good-bye. Get out.**

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*John Abernethy (1764-1831).

**Turner, E. S.: Call the Doctor. St. Martin's Press Inc., New York, 1959.

Character is not made in a crisis — it is only exhibited. — Dr. Robert Freeman

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Problems in Estimating Disability**

ROBERT H. KENNEDY, M.D., F.A.C.S.
New York, New York

Are Workmen's Compensation Laws Outmoded?

DETERMINING PERCENTAGE of disability is a complicated subject. The items to be considered are so numerous and the problems so varied that they should be fed into an IBM machine for computation rather than added to the burden of busy practicing physicians. By definition,* permanent impairment "is a purely medical condition, which is a contributing factor to, but not necessarily an indication of, the extent of a patient's permanent disability. The social and economic effects of permanent impairment must be evaluated by administrators in making determinations of permanent disability."[1] Throughout my surgical career I have declined to estimate percentage disability for any patient's attorney or any insurance company. There are several reasons for this, but one of the most practical is that the figures merely furnish an opportunity for argument among attorneys, claims agents and doctors, whose figures often vary between 10% and 90% disability in the same case. As Kessler, an outstanding specialist in rehabilitation, has said: "No doctor or individual *can* evaluate disability. No man in the world can tell you how much a man is worth, how much work he can do."

Somers and Somers[2] say: "There are two general types of permanent partial disability: (1) those involving the loss or loss-of-use of a readily identifiable member of the body, commonly called 'scheduled' disabilities, and (2) those which cannot be so classified, known as 'non-scheduled' disabilities. Injuries to the back, head, and nervous system are frequent examples of the latter." (However, in Minnesota in 1947 the result of back

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*American Medical Association Committee on Medical Rating of Physical Impairment.

**Presented at Symposium on Disabilities, Virginia, Minnesota, September 20, 1963.

Continued

injuries was made a scheduled disability.) "Compensation involves the difficult problem of determining the degree of incapacity resulting from the injury. Not surprisingly, permanent-partial cases are the cause of a disproportionate share of the administrative tribulations of compensation officials and also represent an inordinately high proportion of benefits."

Schedule awards are completely unscientific. "For example,[3] the loss of an arm in Minnesota is worth 270 weeks, in New York 312 weeks, in Maine 150 weeks, in Vermont 170 weeks, in South Dakota and Texas 200 weeks. Schedule awards merely represent legislative estimates of the proportion that the loss or loss-of-use of a member bears to total disability." "Would[4] you write a mechanical rule categorically stating that loss of hearing is more harmful for all workers than loss of a foot, or vice versa? Workmen's Compensation laws do this, regardless of the occupation, age, and training of the injured worker. In six states, loss of a foot is rated equal to the loss of hearing in both ears; in eleven states, the loss of a foot is rated higher; in 28 states (including Minnesota) deafness is considered more injurious."

The Influence of Liability

In estimating a disability the physician should use the same factors, regardless of the cause of the accident or place of work.

From the economic or insurance viewpoint the following four types of injured individuals must be considered:

1. The injured person who assumes his own financial responsibility: i.e., has no insurance. This person usually recovers most quickly and completely.

2. The injured person who carries accident insurance in some form, e.g., a group policy paid for by his employer, his own accident policy, or Blue Cross and Blue Shield paid for personally or by his employer. Such coverage is held by probably 70% of our population.

3. The employee injured while at work who is covered by compensation insurance. Not more than 20% of accidents will be compensation cases.

4. An individual who is injured off the job under conditions where there may be liability under the common law, or a member of the Armed Forces eligible for Veterans Administration Hospital care, or an individual working for public welfare departments.

Many injured persons are covered by several types of insurance and may be able to use more than one for any given problem.

Evidence of Physical Ability and Employability

A broken leg in a sedentary worker might make little difference in carrying on his job, whereas a longshoreman might need to change his occupation. Facial scars might mean nonacceptability for return as a public relations man or a salesman. McBride[5] says that subjective symptoms, unsupported by clinical evidence of their recent development, should be discounted.

After his condition has been assessed through history, examination, laboratory investigation, and X rays, consideration is given as to how his potential has been altered as a result of the accident.

The extent to which a person will be limited in his work after an accident will depend on his attitude as well as his physical condition. The economic opportunities available will also affect his recovery. He will readjust according to his education and skills. His mental and moral reactions to being dependent on the community, and his willingness to try, all have to be considered. The older person is less able to adjust. Following an accident with permanent partial disability, consideration needs to be given to the safety of the workman himself on his old job, as well as to the safety of others where he is working.

If legislatures or commissions wish to pass laws or regulations regarding rating, they should be responsible for establishing percentages of total disability based on the findings of medical examinations. The compensation laws in most states disregard occupational variations. Loss of earning capacity in ordinary manual labor is recognized; therefore the administrative personnel ought to have authority to adjust the schedule within limits, taking into account various factors about the individual concerned.

Lump-Sum Settlements

There is still too great a tendency to try to buy off the claimant. A lump-sum settlement appeals to the person who has been unable to work for a while, and who with his family is living theoretically on two thirds of his usual income. This figure is an error, since it has been shown repeatedly that the payment is only about half that amount, i.e., one third of his regular income. With few exceptions, "today's injured workers suffer a much greater loss than the early lawmakers contemplated."[6] "The granting of lump-sum payments is an easy, but a deplorable, way of 'closing' a compensation case. It too frequently operates for dissipation of funds and throws the injured employee upon charity in order that he may obtain subsistence. Worst of all is the physical and moral effect of failure on the part of the injured employee to obtain rehabilitation."[7] The settlement is usually for less than the claimant would receive through periodic payments. In Illinois it is estimated that 80-85% of all cash benefits are lump-sum settlements. To the employer and the carrier this is almost always a financial gain. Instead of allowing steady increase in the number of lump-sum settlements, an effort should be made to increase maximum weekly compensation payments. Otherwise this situation could lead to the abolition of private insurance, as happened in England.

Lump-sum settlements offer a multifarious* problem. For example, they lead to false estimates of disability. Theoretically, an estimate should not be made until maximum improvement has been reached, which commonly presupposes providing rehabilitation. To quote from Lane:[3] "It is said that the injured workman must choose between maximizing his injury to increase monetary compensation and minimizing his injury through rehabilitation . . . at the expense of diminishing or terminating his compensation . . . This affords one reason why so few injured workmen seek the benefits of rehabilitation . . . Historically . . . workmen's compensation was a statutory device which its advocates hoped would afford injured workmen a speedy, inexpensive, non-litigious method of securing compensation for industrially caused injuries in place of the common law employers' liability system with its defenses largely weighted in favor of the employer." For those few employees able to establish liability, the judgments were substantial. Regardless of whether we are working under a legal or medical hearing system, rehabilitation should be started on the day the injury occurs.

Monetary Benefits

A factor to be taken into consideration in estimating disability is undoubtedly the common knowledge that the benefits are inadequate, that a workman must frequently borrow money following an occupational injury in order that he and his family may eat. Statutory benefits have not kept pace with the rising cost of living and there has been little sustained effort to increase compensation. These benefits are often even below relief allowances. A variety of programs, both public and private, however, are supplementing or substituting for workmen's compensation. Good labor relations have brought about many of the reforms that compensation was expected to influence. Employees are now safer on the job than off it. Increasingly the whole Social Security program has made the economic function of compensation incongruous.

Supplementary Benefits When Disabled

Some of the programs to "indemnify or offer income maintenance to injured workers and their dependents are:

"1. Private programs compensating for occupational disability or death, financed by employers alone or jointly by employers and workers; . . .

"3. Employers' liability for injured workers in states which permit employers to elect not to be covered by workmen's compensation; (This is not true in Minnesota.)

"4. The common law . . . for domestics,

Continued

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*See Test Your Word Score Page 211.

farmers, and others where excluded from both workmen's compensation and employers' liability;

"5. Federal death and survivorship benefits through OASI and the Railroad Retirement system; . . .

"8. Federal-State public assistance programs, especially Aid to the Totally and Permanently Disabled, Aid to the Blind, and Aid to Dependent Children."[2]

If health insurance, voluntary or compulsory, is adopted, many of the medical needs under workmen's compensation will be covered. Group life, retirement, accident, and health insurance may have a profound effect on the future of workmen's compensation. The unions have been negotiating contracts which cover nonoccupational disability programs with more generous benefits than from workmen's compensation. From overlapping benefits it is often possible in death cases to obtain family payments larger than the deceased's normal earnings. These programs have taken the pressure off workmen's compensation, so that little attempt need be made to improve its inadequacies. Employers without compensation coverage are now seeking to obtain this in order to escape the higher costs of personal injury suits. Efforts are being made to give the injured employee covered under compensation the right to sue where injury was due to negligence of the employer. Some even go as far as suggesting that the employee be allowed to keep both awards.

Conclusions

As laws and directives in workmen's compensation have multiplied, more factors have to be decided by administrators than by doctors. The percentages of disability which many doctors determine are of questionable value. Remuneration under workmen's compensation laws is playing a progressively diminishing part in the economics of the workingman. After 50 years of experience have workmen's compensation laws outlived their usefulness?

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3. Lane, M.: The Effect of the New York Workmen's Compensation Law upon the Employment of the Handicapped. Rehabilitation Monograph XI, Institute of Physical Medicine and Rehabilitation, New York University Medical Center, 1956.
4. Economic Outlook (CIO, Dept. of Education & Research), XIII, 1, Jan. 1952.
5. McBride, E. D.: Disability Evaluation, 5th ed. J. B. Lippincott Co., Philadelphia, 1953.
6. Kossoris in Monthly Labor Review, April 1953, p. 363.
7. Nelson, H. A.: Proceedings of the National Conference on Workmen's Compensation & Rehabilitation. U. S. Bureau of Labor Standards Bull 122: 18, 1950.

Actually, you're never too old to learn. Columbia University psychologists have established that while the most efficient age for learning is between fourteen and twenty-five, thereafter, your ability to absorb new information decreases only one percent per year. At forty-five, you're still able to learn more than you could before the age of fourteen. Even at sixty-five, you still can absorb knowledge half as fast as you could when you were twenty-five. — Hal Burton

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I wrote the following finger exercise in fragments from my past. — Leo Rosten

Abstracts, Briefs and Commentaries

A VIEW OF MEDICINE IN BRITAIN

The Pharos, the official publication of A.O.A., the Honorary Medical Society, has an article of unusual interest by Ernest Craige, M.D. Dr. Craige is a professor of medicine at the University of North Carolina Medical School.

During the year 1963-64, Dr. Craige held a Commonwealth Fund grant to carry out research in congenital heart disease at St. George's Hospital in London. This article reviews in a masterful manner his observations on the aspects of the National Health Service in Great Britain, at present undergoing a critical review, owing largely to the growing discontent among general practitioners. The present wave of indignation is in part due to the promised hike in pay which fell well below that anticipated. However, mounting protests in the British Medical Journal and in the lay press indicate a deeper discontent than remuneration alone. Conditions of practice and apprehension over the whole future of the profession are fundamental. Under the plans of organization of the National Health Service, general practitioners insisted they should remain independent professional men rather than salaried employees. They are paid an annual total based on the number of patients on their lists (maximum 350), with a few ways of supplementing earnings. The general practitioner fees are derived from a central pool which averages out at about 2742 pounds (less than $7000), plus an estimated amount for expenses of practice. A minor amount taken from the pool for extra service before division into shares penalizes the group and creates unhappiness.

Any payments for office renovations, secretarial or laboratory ancillary help must come out of gross pay. The estimated cost of practice expense based on a national average may be inadequate, and there is no provision for capital improvements. One partnership recently improved their surgery (office) at an expense of 2000 pounds. They received no reimbursement for the outlay, and were shocked to find their taxes had gone up because of the improvements.

Many general practitioners have no hospital privileges, which widens the gulf between them and those who have. They complain that their duties

Continued

consist more of filling out certificates for inability to work, free appliances, and sorting out from the mass of patients those who are really sick and who are sent to the hospital for consultant's care. General practitioners are discouraged by the large number of office patients to be seen and the cost of extra studies which comes from their gross income. Since income per service rendered constitutes on the average only six shillings (84¢), there is little inclination to provide elaborate technical studies. In spite of these conditions, however, many general practitioners perform admirable service.

"Letters to the British Medical Journal speak of the disillusionment of general practice, a blind alley occupation, or a dead end." In spite of this, however, the severe critics seem to have no desire to return to the preexisting system. Consultation and elaborate studies by consultants cost the patient nothing regardless of his ability to pay.

As a medical student nears graduation he chooses between general practice and consultant practice. In either case he applies for a position of house physician (intern) in as good a hospital as possible. Following a year or two of training the trainee becoming a general practitioner may seek a post as assistant to a practitioner and later obtain an appointment as a principal in the National Health Service with his own practice. If he elects to stay in hospital training with a goal of consultant, he must take a succession of jobs in general medicine and surgery and finally enter a more specialized field. After seven to 12 years he may acquire the status of consultant. "This, however, can only occur when an existing post becomes vacant upon the death or retirement of the incumbent." In view of the fact that there are many persons seeking this appointment, he finds he has completed a prolonged training program that is over-subscribed with an endless period of frustration and waiting. A consultant may have assistants (registrars) who have had years of preparation, who became teachers or researchers, and who have a private practice. The author observed some registrars with five to nine years following graduation without promotion. Some emigrate rather than wait longer for promotion. Like the general practitioner, they dare not complain, as their promotion to consultant depends on the goodwill of those in authority.

Hospital construction has been neglected and almost half of the hospitals in Britain are over 70 years old.

In summary, the author states that there are, nevertheless, some good achievements. After 16 years, the National Health Service has not devised a system that satisfies the general practitioner intellectually or financially, as evidenced by falling recruitment plus the migration of frustrated young graduates. But he suspects that as the older general practitioners— "products of an earlier mold" drop out, they will be replaced by new younger ones, who having known nothing different will be more contented civil servants. "Therefore, it seems to me more likely that the general practitioner will suffer an invertebrate evolution rather than the National Health Service a revolution."

"From this rather gloomy view, one needn't derive a sense of complacency with regard to the American scene." He believes there is strength in the diversity of our methods. General practitioners have freedom. Some of his British friends blame the inadequacies of their system not on the government planners but on the ineptitude and lack of vision on the part of the professional negotiators.

Discussion

In the May issue of Minnesota Medicine I reviewed an article published in the Lancet— "Status of Medical Practice in England." This review, although similar, is such a fine presentation written by one of our outstanding teachers, based on one-year observations, and seems unusually timely. There are several quotes which I consider worthy of serious consideration by our medical profession. The inroads of socialization in government and medicine are obvious. Let our profession and its governing bodies not be accused of ineptitude and lack of vision.

In hopes that I may not be considered overly critical in these reviews, may I state that during my two years in service with the British, I developed a deep respect for them, their sincerity, and their loyalty, but less for their system of medicine.

Stanley R. Maxeiner, M.D.
Minneapolis, Minnesota

IRRADIATION TREATMENT FOR PEPTIC ULCER

X-ray irradiation of the stomach in the treatment of peptic ulcer was first suggested in 1909, and by 1935 over 200 papers had been published on this treatment. Careful studies on thousands of patients have established that irradiation reduced the recurrence rate to one fifth and hastened healing. Nevertheless, this use of irradiation is not generally known and has not been widely adopted. Many prefer surgery despite its risks and the dumping syndrome it often produces..

The technique of irradiation is simple: the stomach is outlined with barium and the skin marked during fluoroscopy. An anterior and posterior field is centered over the upper two thirds of the stomach (where the acid-secreting cells are). An irradiation dose of 2000 r. is given through each port in six to eight treatments. In most institutions the 250-kv. apparatus is used.

Results are reported in 121 patients with complicated peptic ulcer, 79 of whom have been followed up for over four years, after cobalt 60 teletherapy. The reactions were minimal.

A total of 629 gastric secretion studies were done. In 90 percent of the patients the basal gastric secretion was reduced more than 50 percent in the first six months, though hyperacidity usually recurred after six months to one year. In 87 cases the ulcer did not recur; in 13 there was a questionable recurrence and in 21 a definite recurrence.

Cobalt 60 teletherapy is a very useful method of treating peptic ulcer, especially in cases where cardiac lesions, hypertension or other complications contraindicate surgery.

Courtesy of World-Wide Abstracts

Brown, C.: Amer J Gastroent 38/3:278

SYMPATHECTOMY FOR FROSTBITE

A well controlled laboratory study has been conducted by the authors to evaluate the effect of sympathectomy in the frozen hind leg of rabbits. In addition to the controlled group with no sympathectomy, three other groups were studied, one with a sympathectomy three days prior to freezing injury; another within one hour after freezing and thawing; and finally another group 24 hours thereafter. A definite improvement in tissue survival followed sympathectomy when accomplished as quickly as possible after the freezing and thawing procedure.

The authors point out that immediately after thawing there is a transient vascular spasm followed within a few minutes by resumption of blood flow, then by an appearance of hyperemia with decreased and finally absent flow within the capillaries. This was followed ultimately by a thrombosis if the spasm is unconnected. A venous spasm lasts up to 24 hours, but arteriolar spasm remains beyond that point. They also point out that rapid thawing of the frozen tissue improves the degree of tissue survival, and suggest an optimal temperature of 42 to 43 degrees centigrade.

No clinical human studies have been done by these authors on this particular procedure. However, it would seem well established that timing of the sympathectomy is very significant.

J. H. Strickler, M.D.
Minneapolis, Minnesota

Gildenburg, Philip L., and Hardenbergh, Esther: The Effect of Immediate Sympathectomy on Tissue Survival Following Experimental Frostbite. Ann Surg 160:160, 1964.

COMMUNITY-WIDE EXPERIENCE WITH LIVE VIRUS MEASLES VACCINE

The two physicians of Cook County, Minnesota, enlisted the help of local citizens to provide a measles immunization program for the 1416 school children in this isolated community. As reported by R. A. MacDonald, M.D., of Grand Marais, efforts to promote measles immunization on a private patient basis were slowed by professional reluctance to "advertise" the vaccine and relatively high cost on a per unit basis. Working with local health organizations, two lay groups ultimately underwrote the cost of the project and volunteer workers assisted professional nurses in arranging clinics, and making follow-up visits to all vaccinated children.

For $3.00 each child received live virus vaccine at a dose 0.01 ml. per pound plus gamma globulin. Infants less than 11 months of age were excluded in order to avoid abortive immunizations. Of 1349 children from one to 18 years old, 564 gave a history of rubeola, and were thus considered immune. Of those nonimmune, 454 received the vaccine, and thus 74% of the school population were then considered immune. There were 10 reactions, mainly mild rubeola; convulsions occurred four hours after injection of an eight-year-old boy found to have an unsuspected acute tonsillitis. There were no allergic reactions.

This report demonstrates again the remarkable results achievable when physicians and laymen work together toward a common goal.

John V. Thomas, M.D.
Duluth, Minnesota

SPRAINED ANKLE

Of a total of 103 acutely injured ankles seen by the author during a six-month period, 85 presented simple sprain, and 18 were fractured. This proportion does not represent the true incidence of ankle fracture, for a number of patients were referred directly to a fracture clinic. To diagnose the extent and seriousness of the injury, a brief medical history was taken and the ankle was first examined clinically. A careful note was made of the exact site of swelling and of tenderness, in relation to the ligamentous attachments and the bony points. The ankle was exposed to a full range of passive movements, and any limitation, or any increase, in range was evaluated by comparison with the patient's normal ankle. Only if the affected ankle showed a greater range of inversion than the normal, or if there was tenderness over the attachments of the calcaneofibular ligaments, were X ray pictures of the anteroposterior and lateral views taken. The patients were treated at random with adhesive strapping (30 patients) and by injection of hyaluronidase into the injured ligament (38). In three quarters of the hyaluronidase-treated group the therapy resulted in pain-free walking in less than half the time taken for a similar proportion of patients treated with adhesive strapping to achieve similar results. The severity of the injury, the patient's age, and the interval between the trauma and the treatment may have influenced the results. A follow-up two years after the treatment indicated that the short-term advantages were not outweighed by any long-term disadvantages. In none of the patients available for the follow-up did failure to immobilize a sprained ankle result in any serious long-term disability.

Courtesy of References and Reviews
Journal of the American Medical Association

Lettin, A.: Brit Med J 1:1056 April 20, 1963

VAGINAL METASTASES FOLLOWING TREATMENT OF ENDOMETRIAL CARCINOMA

These authors report 269 cases of endometrial carcinoma in which they observed a post-treatment vaginal metastases incidence of 4.4%. This low incidence when compared to other published reports is attributed by the authors to preoperative prophylactic radiation therapy to the uterus and upper vagina.

Evaluation of the histologic patterns of the primary lesions showed an apparently higher incidence of vaginal metastases when the carcinoma was poorly differentiated or when deep myometrial or lower uterine segment extension of the lesion was present. Virtually no vaginal recurrences after treatment appeared if the primary lesion was confined to the endometrium or was of an early well-differentiated histologic pattern.

The incidence of vaginal recurrence was nearly identical among patients treated with radium (3.7%) or with radiation and surgery (3.8%). Vaginal metastases subsequently developed in five or 26.3% of 19 patients treated by surgery alone.

Continued

Treatment of the vaginal recurrences was individualized and related to location of the lesion. Most were treated by intravaginal radium and external radiation. Two underwent vaginectomy. The over-all five-year survival rate among those with vaginal metastases was 27.2%.

On the basis of the data presented, the authors plead for prophylactic preoperative radiation in the treatment of endometrial carcinoma to reduce the incidence of subsequent vaginal metastases.

Discussion: Vaginal recurrence subsequent to treatment for adenocarcinoma of the endometrium is certainly not a rare occurrence. It appears at some time or another in about 10% of the patients with this disease. The possibility of vaginal recurrence should always be considered before primary treatment is begun. Appropriate modification of standard therapeutic techniques is indicated to lessen the chance of vaginal recurrence among patients who are predisposed to this complication. Many articles in addition to this one have demonstrated that certain patients are more likely to develop post-treatment vaginal recurrence than others. In addition to the anaplastic lesion or the lesion which deeply invades the myometrium or extends into the lower uterine segment as mentioned in the reviewed article, experience at the University of Minnesota has shown that extension of the primary lesion downward into the cervical canal also carries a very high risk of post-treatment recurrence. The identification of cervical canal extension is not difficult if the patient with suspected endometrial adenocarcinoma is subjected to a differential or fractional curettage of the uterine cervix and corpus for an exact and detailed diagnosis.

Most gynecologists experienced with this problem agree that intensive preoperative radiation is indeed indicated to reduce the incidence of subsequent vaginal metastases and also pelvic recurrence not only in the high-risk patient categories suggested by the authors but also in the patient with endocervical extension. The patient, however, who has a small, mobile uterus and a superficial highly-differentiated lesion need not and should not be routinely subjected to preoperative radiation. The prognosis for complete cure by simple hysterectomy and removal of the adnexa in this type of lesion is excellent and the prospect for subsequent vaginal recurrence is almost nil even without preoperative radium and external radiation therapy.

The high incidence reported in the article of vaginal recurrence among patients treated only with surgery does not reflect the experience at the University of Minnesota where the vaginal recurrence rate after hysterectomy is 8-10 per cent. The number of cases reported by the authors in the abstracted article is too small to be of true value in analyzing the magnitude of the problem and to compare with larger groups of patients treated in a similar manner.

The prognosis for the patient with post-treatment vaginal recurrence is not a hopeless one. Several reports have shown a 25-50 per cent five-year survival rate after appropriate treatment to the lesion has been administered.

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Dept. of Obstetrics and Gynecology
University of Minnesota

Boutselis, John G., Ullery, John C., and Bair, J.: Obstet Gynec 21:622, 1963.

WIDE LYMPH NODE DISSECTION FOR CARCINOMA OF LEFT HALF OF COLON

Bacon and Khubchandani have extended the lymph node dissection for left colon carcinoma to the root of the inferior mesenteric artery, and have also included sectioning of the inferior mesenteric artery. They have pointed out that without this extensive lymph node dissection their studies indicate that nine per cent of all the operations by the usual method would have left involvement of lymph nodes. They carry out this procedure for the cure of patients with cancer of the descending colon, the sigmoid, rectum, and anal canal and the only contraindications are in elderly patients, poor-risk patients, and patients with extreme obesity. Though the operation is somewhat prolonged, the morbidity was not particularly greater than that associated with the conventional type of operation.

Depending upon the site of the lesion, the percentage of improvement in the five-year survival was from four to ten per cent. The greatest improvement was observed in patients when the malignancy was located in the descending colon or sigmoid. The authors were able to conclude that there was no danger in lowering the blood supply, and that there was adequate collateral circulation from the superior mesentery to keep the anastomosed tissues viable.

They suggest the hope that in the future it will be possible to detect the involved lymphatic chain preoperatively and perform a selective lymphadenectomy.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Bacon, Harry E., and Khubchandani, Indru T.: The Rationale of Aortoiliopelvic Lymphadenectomy and High Ligation of the Inferior Mesenteric Artery for Carcinoma of the Left Half of the Colon and Rectum. SG&O 119:503, 1964.

The Primitive Medicine Man

The medicine man was especially selected. Usually he was marked out from birth. In Liberia twins are regarded as particularly gifted. Seventh sons, as is well known, are attuned to the whisperings of the infinite. And, of course, the seventh son of a seventh son is doubly dyed. One such, a fiery old fellow, in the Highlands of Scotland, who was a militant atheist, was nevertheless up to a few years ago constantly besieged by his neighbors and even awakened in the dead of night to touch sick people brought to his door. (Logan Clendening)*

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*Rapport, Samuel, and Wright, Helen: Great Adventures in Medicine. The Dial Press, New York, 1952, p. 40.

No one grows old by merely living a number of years; they grow old only by deserting their ideals. Years may wrinkle the skin, but to give up enthusiasm wrinkles the soul. — Long Lines

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A man is as big as the things that annoy him.

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SIDE EFFECTS: Blurring of vision, dry mouth, difficult urination or flushing and dryness of the skin may occur at higher dosage levels, rarely at the usual dose.

*This one at Oak Creek, Castle Rock, Arizona

References: 1. Hock, C. W.: Clin. Med. 8:1932, 1961. 2. Marks, L.: Am. J. Gastroenterol. 27:180, 1957. 3. Palmer, W. L., and Kirsner, J. B.: Therapeutics in Internal Medicine, 2nd ed., F. A. Kyser, Ed., Hoeber, New York, 1953, p. 368. 4. Ryan, J. P., Jenkins, H. J. and Robinson, S. M.: J. Pharmaceut. Sciences 53(9):1084, 1964. 5. Vollmer, H.: Arch. Neurol. & Psychiat. 43:1057, 1940. Abst. J.A.M.A. 115:333, 1940. 6. Wharton, G. K., Balfour, D. C., Jr., and Osman, K. I.: Postgrad Med. 21:406, 1957.

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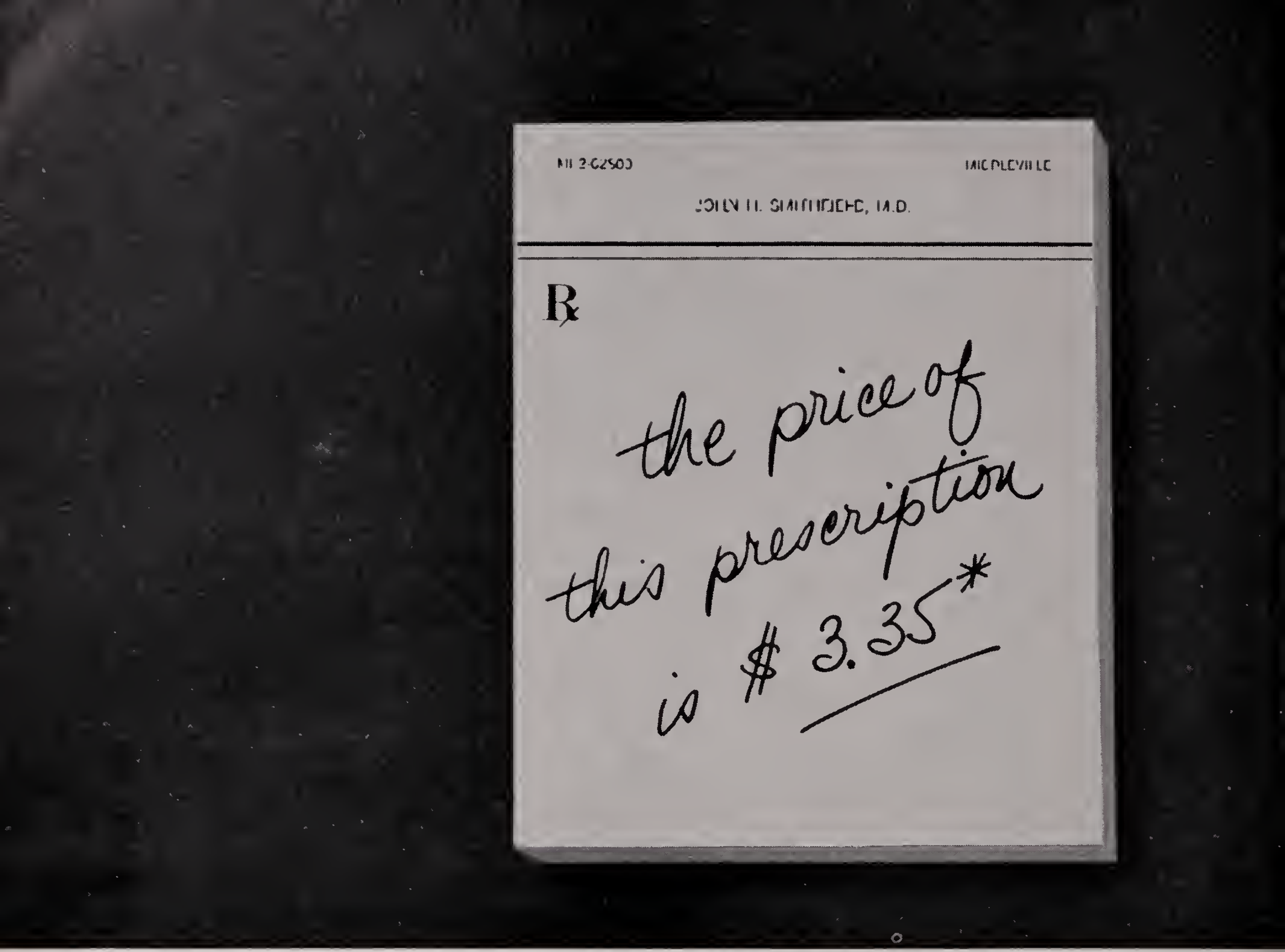

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Somewhat amazingly, $3.18 is correct. Even if you eliminated pharmaceutical manufacturer's net profit, your patient would pay only about 17 cents less for the average prescription—hardly a deciding factor in having it filled. Of course, this assumes that pharmaceuticals could continue to be available without profit (where do new miracle drugs come from, if not profit?).

American pharmaceuticals today may well be America's biggest bargain.

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This message is brought to you as a courtesy of this publication on behalf of the producers of prescription drugs.

*Average prescription price, 1963. National Prescription Audit, R.A. Gosselin, Dedham, Mass.

Book Reviews

My books kept me from the ring, the dog-pit, the tavern, and the saloon. — The associate of Pope and Addison, the mind accustomed to the noble though silent discourse of Shakespeare and Milton, will hardly seek or put up with low or evil company and slaves. — Thomas Hood

AN ATLAS OF VASCULAR RINGS AND RELATED MALFORMATIONS OF THE AORTIC ARCH SYSTEM — **James R. Stewart, Owings W. Kinkaid and Jesse E. Edwards. Springfield, Ill., Charles C. Thomas, 1964. 155 pages, index, 216 illus., references.**

Embryology, roentgenology and pathology are welded to form an atlas and classification system of disorders pertinent to the study of peripheral vascular disease. The authors are from the Departments of Roentgenology and Pathology of the University of Minnesota. Dr. Edwards is the author of An Atlas of Acquired Diseases of the Heart and Great Vessels.

A hypothetical model in which none of the developmental regressions of the aortic arch system have taken place is used as a reference point. Division then follows — dependent on position of the aortic arch and the presence of ducti arteriosi. Each condition is illustrated with a drawing of the embryologic origin of the vasculature, photographs of the pathologic specimen and skiagrams when available. There are brief clinical notes.

The atlas succeeds in presenting to clinicians and to others concerned with developmental biology a highly technical and informative study of anomalies of the aortic arch system. Organization is that of the classification system, and makes for easy reference and ready understanding of the morphology. Illustrations are adequate and well reproduced; an extensive bibliography is provided.

George E. Kitzmiller, M.D.
Hennepin County General Hospital
Minneapolis, Minn.

"SIGNS AND SYMPTOMS" — **Cyril Mitchell MacBryde, J. B. Litman Co., 1964. 971 pages.**

This is Fourth Edition of MacBryde's "Signs and Symptoms."

The word symptom is used to name a manifestation of disease, which is usually a subjective observation from the patient.

Pain being a significant sign, the book contains eight chapters dealing with pain, originating from the various sections of the body. By using the table of contents, the reader is able to guide himself into the proper chapter, which may be of interest to him at the moment.

Generalized vasospasm, tachycardia, cough, hemoptysis, dyspnea and cyanosis, direct the reader to a series of chapters devoted principally to cardiovascular and respiratory disease, and then there are a series of signs which direct one to the diseases of the gastrointestinal and biliary system.

Bibliographical references are tendered at the end of each chapter and these, though not extensive, seem to be adequate for more specific reference to the contents within each chapter.

I have found this to be an excellent edition, as a reference for a large variety of signs and symptoms that one encounters from day to day.

Carl O. Rice, M.D.
Minneapolis, Minnesota

OCULAR AND ADNEXAL TUMORS — **New and Controversial Aspects, Edited by Milton Boniuk, M.D., C. V. Mosby Co., St. Louis, 1964. 511 pages. Illustrated, references, index. Price $25.00.**

This beautiful volume contains the papers and discussion of the International Symposium on Ocular Tumors, sponsored by Baylor University College of Medicine in 1962. The book has been divided into four sections—tumors of the conjunctiva and eyelid, retinoblastoma, pigmented intraocular tumors, and orbital tumors. We find here, well edited and illustrated, the most recent information regarding the incidence, clinical and pathological diagnosis, and management of ocular and adnexal neoplasma.

This book contains a complete list of references, and would be of value to the pathologist, neurosurgeon, and ophthalmologist.

William S. McClanahan, M.D.
Minneapolis, Minnesota

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Nicotinic Acid .... 75 mg.
Glycine ....750 mg.

REFERENCES:

1. Goodgold, J., Use of Nicotinic Acid-Glycine Mixture in Treatment of Peripheral Vascular Disease, Clinical Medicine 7:12 (1960).
2. Gustafson, Jr. et al. Use of Glycine in the Treatment of Peripheral Vascular Disease, Surgery 25:539 (1949).

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Classified advertising rates are twenty (20) cents a word; minimum monthly charge $5.00; key number, fifty (50) cents additional.

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WANTED general practitioner for locum tenens for the month of February, 1965. Modern hospital and clinic, consultation available. Will pay $1,200 for the month. Write or call collect: William C. Heiam, M.D.; Cook, Minnesota.

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Minnesota State Board of Medical Examiners

Notice of Public Hearing
Minnesota State Board of Medical Examiners

"Notice is hereby given, pursuant to the provisions of Minnesota Statutes, 1961, S 15.0412, that the Minnesota State Board of Medical Examiners will hold a public hearing on Saturday, February 13, 1965, at 10 o'clock, A.M., in the auditorium of the State Office Building, Saint Paul, Minnesota, on the adoption of proposed substantive rules and regulations pertaining to professional corporations and to the practice of medicine and surgery, osteopathy, massage, physical therapy and midwifery, and of procedural rules and regulations pertaining to the hearing of contested cases before the Minnesota State Board of Medical Examiners.

Copies of the proposed procedural and substantive rules and regulations are available from the Secretary of the Minnesota State Board of Medical Examiners, 230 Lowry Medical Arts Building, Saint Paul, Minnesota, 55102.

Interested persons are invited to attend and submit data or views orally or in writing.

Dated at Saint Paul, Minnesota, this 23rd day of November, 1964.

By Order of the Minnesota State Board of Medical Examiners

J. P. Medelman M.D.

Secretary-Treasurer"

Rules and Regulations Pertaining to the Practice of Medicine, Surgery, Osteopathy, Physical Therapy, Massage and Midwifery, Proposed by the Minnesota State Board of Medical Examiners on November 19, 1964, Pursuant to Authority Conferred by Minnesota Statutes Annotated, Sections 147.01, 148.30-148.511, inclusive, 148.65-148.78, inclusive, and Sections 15.0411-15.0415, inclusive.

The following rules are adopted to carry out the purpose and intent of M.S.A., c. 147, §§ 148.30-148.511, inclusive, and 148.65-148.78, inclusive.

Rule 1. Definitions

1.01 As used in M.S.A., c. 147, and M.S.A., §§ 148.30-148.511, inclusive, and 148.65-148.78, inclusive, the terms herein defined shall have the following meanings:

1.011 "Minor surgery," as used in M.S.A., § 147.031, subd. 2, relating to the practice of osteopathy shall be construed to include all surgical procedures excepting: (a) those involved in incision for the opening of a natural body cavity, (b) open reduction of bone fractures, (c) the amputation of an extremity or an appendage, (d) the removal of any gland or organ or part thereof, or (e) any plastic surgery.

1.012 "Anesthetics," as used in M.S.A.,

Continued

§ 147.031, subd. 2, shall mean and include any agent used to produce topical, local, or general anesthesia. Such agents shall include, but shall not be limited to, the following: cyclopropane, ether, ethylene, chloroform, pentothal, barbiturates, nitrous oxide, cocaine, procaine, or any other agent intended to produce a like effect.

1.013 "Narcotics," as used in M.S.A., § 147.031, subd. 2, shall have the meaning ascribed to the term "narcotic drugs" by 26 U.S.C.A., § 4731, and by M.S.A., § 618.01, subd. 14. A narcotic drug includes, but shall not be limited to, the drugs specifically referred to in 26 U.S. C.A., § 4731, M.S.A., § 618.01, subd. 14, any compound derivative or preparation of the same, and any substance having an addiction-forming or addiction-sustaining liability similar to any of the same or capable of conversion into a drug having such addiction-forming or addiction-sustaining liability.

1.014 "Antidote," as used in M.S.A., § 147.031, subd. 2, shall mean any agent used to counteract the effects of a poison.

1.015 "Antiseptics," as used in M.S.A., § 147.031, subd. 2, shall mean any chemical or biological agent used to destroy or inhibit the growth and development in living tissue of microorganisms, and includes, but shall not be limited to, antiseptic agents defined as such in the official United States Pharmacopoeia, or registered and regulated for distribution under 21 U.S.C.A., §§ 351-357, inclusive.

1.016 The "Board" as used in these regulations shall mean Minnesota State Board of Medical Examiners.

1.017 The "Examining Committee" as used in these regulations shall mean the State Examining Committee for Physical Therapists created by M.S.A., § 148.67.

Rule 2. Application for Licensure for Medicine and Surgery

2.01 *Application.* An application for admission to a licensing examination to practice medicine shall be filed with the Board as hereinafter prescribed. If the Board finds that the application is complete and that all of the requirements of M.S.A., § 147.02, and of these regulations have been met, it shall advise the applicant of the date and place of the examination.

2.02 Such application shall be submitted on forms prepared by the Board and shall include the following information:

2.021 Original or certified copy of diploma from a medical or osteopathic college, as the case may be, duly accredited by the Board, indicating that the applicant has satisfactorily completed a course of study acceptable to the Board and that he has received from such college the degree of Doctor of Medicine, Bachelor of Medicine, Bachelor of Medicine and Surgery, or Doctor of Osteopathy.

2.022 Evidence, satisfactory to the Board, that the applicant has satisfactorily completed at least twelve (12) months of graduate training in a hospital approved by the Board.

2.023 A certificate of registration in the basic sciences issued by the Minnesota State Board of Examiners in the Basic Sciences.

2.024 A certificate of good moral character signed by two persons licensed by any recognized and accredited licensing authority within the United States or Canada to practice medicine and surgery.

2.025 An unmounted recent photograph of applicant with an affidavit on the reverse side thereof made by the applicant that the photograph is that of the applicant.

2.026 Such other information as the Board shall, from time to time, deem necessary in order to evaluate the qualifications of the applicant.

2.03 *Hearing on Applications.* An applicant whose credentials are determined by the Board to indicate ineligibility for examination shall be notified of such determination and the grounds therefor and may file with the Board a formal petition setting forth such grounds as he may desire in support of his eligibility. The Board shall, after due consideration of such petition, determine the merits of the petition and forthwith notify the applicant of its decision.

2.04 All applications for examination must be fully completed and forwarded to the Secretary of the Board, postmarked not later than thirty (30) days before the date of the examination.

Rule 3. Conduct of Examinations

3.01 Examinations shall be both written and oral. A written examination shall be given in surgery, medicine, materia medica, pediatrics, eye, ear, nose and throat, obstetrics, gynecology, and such other branches as the Board may from time to time determine.

3.02 Licensing examinations shall be conducted in accordance with the following rules, and any candidate violating such rules may be dismissed and barred from taking the examination, or may be otherwise disciplined.

3.021 During the written examination no applicant shall communicate with any other applicant in any way except with the express permission of the person or persons conducting the examination.

3.022 An applicant shall not bring books or help of any kind into the examination room.

3.03 *Grading of the Examination.* A grade of 75 shall be the passing grade. A minimum general average of 75 in all subjects shall constitute a grade satisfactory for licensure. An applicant may fall below 75 in one subject and still be licensed by the Board. If an applicant falls below 75 in more than two subjects, it shall constitute a failure and require that the applicant retake the entire examination with passing grades in order to be eligible for licensure. An applicant failing two subjects may retake the two subjects at the next examination and upon receiving a minimum grade of 75 in each may be eligible for licensure.

3.04 Upon the conclusion and grading of the examination, the Board shall prepare a report of the examination results, and shall act on the report at its next meeting. The Secretary of the Board shall notify the applicant of the action of the Board on his application and examination.

Rule 4. License by Reciprocity to Practice Medicine and Surgery

4.01 An application for a license to practice medicine and surgery, without written examination, in accordance with M.S.A., § 147.03, may be made by any physician duly licensed by an accredited state licensing board or agency.

4.02 Such application shall be submitted on forms prepared by the Board and shall include the following information:

4.021 An original or certified copy of all of applicant's then current licenses, including the license originally obtained by examination, together with evidence at the time of submission that all of the same are in good standing.

4.022 Original or certified copy of certificate of registration in the basic sciences issued by The Minnesota State Board of Examiners in the Basic Sciences.

4.023 Original or certified copy of diploma from a medical or osteopathic college, as the case may be, duly accredited by the Board, indicating that the applicant has satisfactorily completed a course of study acceptable to the Board, and that he has received from such college the degree of Doctor of Medicine, Bachelor of Medicine, Bachelor of Medicine and Surgery or Doctor of Osteopathy.

4.024 Evidence, satisfactory to the Board, that the applicant has satisfactorily completed at least twelve (12) months of graduate training in a hospital approved by the Board.

4.025 An unmounted recent photograph of applicant with an affidavit on the reverse side thereof made by the applicant that the photograph is that of the applicant.

4.026 A certificate of good moral character signed by two persons licensed by any recognized and accredited licensing authority within the United States or Canada to practice medicine and surgery.

4.027 Such other information as the Board shall, from time to time, deem necessary in order to evaluate the qualifications of the applicant.

Continued

Rule 5. License by Endorsement without Examination to Practice Medicine and Surgery

5.01 An application for a license to practice medicine and surgery by endorsement, without examination, may be made by any applicant who has passed an examination given by the National Board of Medical Examiners, the National Board of Examiners for Osteopathic Physicians and Surgeons, or by the appropriate board or agency of any state or country which the Board may from time to time determine to be acceptable, as provided in M.S.A., § 147.03; provided, however, that the Board may require the applicant to be examined in such subjects which, in the opinion of the Board, have not been satisfactorily covered, and may require the applicant to pass an oral examination.

5.02 Such application shall be submitted on forms prepared by the Board and shall show the information required by Rules 4.022 through 4.026, inclusive, and in addition thereto, the original or certified copy of the certificate or diploma from the appropriate national or state board or agency, as referred to in Rule 5.01 hereof, evidencing satisfactory completion of the examination therein referred to.

Rule 6. Temporary Permits to Practice Medicine and Temporary Certificates for Graduate Training

6.01 Applications for a temporary permit to practice medicine, pursuant to the provisions of M.S.A., § 147.02, shall be submitted on forms prepared by the Board and shall include the information required by Rule 4.02.

6.02 An application for a temporary certificate for graduate training, pursuant to the provisions of M.S.A., § 147.16, shall be submitted on forms prepared by the Board, which shall include the following information:

6.021 Original or certified copy of birth certificate.

6.022 Evidence of good moral character satisfactory to the Board.

6.023 Original or certified copy of degree, certificate or diploma from a school approved by the Board or evaluating agency recognized by the Board, evidencing satisfactory completion of a course of study as described in M.S.A., § 147.02.

6.024 In the case of an applicant whose course of study was completed at a school outside of the United States or Canada, evidence satisfactory to the Board that the school or college issuing the degree is approved by the licensing authority of the jurisdiction or country in which such medical or osteopathic school is located.

6.025 Original or certified copy of license to practice medicine in all of its branches in the state, territory or foreign country in which applicant resides or, if applicant is not so licensed, evidence satisfactory to the Board that applicant has passed an examination, or is eligible therefor, which is substantially equivalent to the examination given by the Board to applicants for a license to practice medicine in all of its branches in Minnesota.

6.026 Original or certified copy of certificate of registration in the basic sciences issued by The Minnesota State Board of Examiners in the Basic Sciences.

6.027 In the case of an applicant for residency training, evidence satisfactory to the Board that said applicant has completed at least twelve (12) months of hospital training as an intern in a hospital acceptable to the Board.

6.028 The name and location of the hospital at which such graduate training will be taken, and evidence that the hospital has accepted the applicant for training.

6.03 Upon issuance of a temporary certificate for graduate training, the holder may take postgraduate training in a teaching hospital within the State of Minnesota approved for resident training by the Board.

6.04 The holder of such certificate may perform those services incident to the training prescribed by the approved hospitals while acting under the direction of a person licensed to practice medicine and surgery in this state; provided, however, that no fee or remuneration of any kind shall be collected by the holder of such certificates from any patients treated by him; and, provided, further, that said holder of the certificate shall confine his training and practice to the hospital or group of hospitals designated in his original application.

Rule 7. Requirements for Licensure of Foreign Graduates in Medicine and Surgery

7.01 A graduate of a foreign medical school may apply for licensure to practice medicine and surgery in Minnesota, in accordance with M.S.A., § 147.02, by filing with the Board an application on forms provided by the Board, which forms shall include the following information:

7.011 The information required by Rules 2.023, 2.025 and 2.026.

7.012 Evidence satisfactory to the Board that the applicant is a graduate of a foreign medical school and is the holder of an approved diploma or degree recognized by the Board as evidencing a level of training from said approved foreign medical school commensurate with the medical training required by approved medical schools in the United States.

7.013 In the event that the applicant is not a citizen, he shall submit with his application evidence that he has made a declaration of intent to become a citizen of the United States.

7.014 Original, or certified copy, of his license to practice medicine and surgery in the foreign country, issued by the school from which he graduated or by the appropriate licensing body of the country in which he was originally licensed.

7.015 Evidence that the applicant, at the time of his application, is the holder of a valid license to practice medicine and surgery in the foreign country in which he is then residing.

7.016 Evidence of good moral character satisfactory to the Board.

7.017 Evidence of satisfactory completion of two (2) years training in an institution in Minnesota approved by the Board, or training, in the opinion of the Board, equivalent thereto.

Rule 8. Procedure for Licensure to Practice Medicine and Surgery by Persons Licensed to Practice Osteopathy

8.01 Any person licensed to practice osteopathy in this state under M.S.A., §§ 148.11 to 148.16, inclusive, may apply to this Board to be examined for licensure to practice medicine and surgery by filing with the Board an application on forms provided by the Board setting forth the date on which the applicant was licensed to practice, the number of years and place or places in which he has practiced.

8.02 The applicant, prior to licensure to practice medicine and surgery, shall be required to pass an examination in those subjects described in Rule 3.01 hereof in which the applicant has not previously been examined.

8.03 All applications, together with supporting credentials, shall be completed and filed with the Secretary of the Board at least thirty (30) days prior to the examination.

8.04 *Grading of the Examination.* A grade of 75 is considered to be the passing grade. A minimum general average of 75 in all subjects constitutes a grade satisfactory for licensure. An applicant may fall below 75 in one subject and still be licensed by the Board. If an applicant falls below 75 in more than two subjects, it shall constitute a failure and require that the applicant retake the entire examination with satisfactory grades in order to be eligible for licensure. An applicant failing two subjects may retake the two subjects at the next examination and upon receiving a minimum grade of 75 in each may be eligible for licensure.

Rule 9. Physical Therapy—Regulations Governing Registration and Practice

9.01 *Application.* An application for admission to a registration examination to practice physical therapy shall be filed with the Board as hereinafter prescribed. If the Board finds that the application is complete and that all of the requirements of the statute and of these regulations have been met, it shall advise the applicant of the date and place of the examination.

9.02 The application shall require the applicant to submit the following information:

9.021 Original or certified copy of birth certificate.

9.022 Original or certified copy of high

Continued

school diploma or evidence of equivalent education.

9.023 Original or certified copy of diploma, degree or certificate, or evidence satisfactory to the Board, indicating that the applicant has satisfactorily completed an approved curriculum in physical therapy as provided in M.S.A., § 148.70(d) and has graduated from a school of physical therapy approved by the Board and having standards of education and training substantially equivalent to the standards and training of the University of Minnesota.

9.024 Evidence, satisfactory to the Board, that the applicant is of good moral character.

9.025 An unmounted recent photograph with the affidavit of the applicant on the reverse side thereof that the photograph is that of the applicant.

9.03 An applicant, prior to registration, shall be examined in the subject matter described in M.S.A., § 148.70(d), and a listing of the subjects to be covered shall be made available by the Board to the applicant. Such examination may be oral, written, or both, and shall be conducted by the Board with the assistance of the State Examining Committee.

9.04 The Board may register as a physical therapist in this state without examination any person who presents evidence satisfactory to the Board of having passed an examination in accordance with the provisions of M.S.A., § 148.72, subd. 2, administered by a duly accredited examining agency. An applicant for registration without examination shall submit on forms provided by the Board the following information:

9.041 Original or certified copy of high school diploma, transcript of high school credits, or evidence of equivalent education.

9.042 Original or certified copy of diploma, degree or certificate of completion of an approved course in physical therapy.

9.043 Original or certified copy of birth certificate.

9.044 Original or certified copy of current license or certificate to practice physical therapy, if any, issued by the duly accredited examining agency of the state or foreign country from which the applicant is seeking registration without examination.

9.04 Unmounted recent photograph of applicant with an affidavit on the reverse side thereof made by the applicant that the photograph is that of the applicant.

9.04 A recommendation of good moral character by one physician and one physical therapist, each duly registered to practice medicine and physical therapy in the United States or Canada.

9.04 Complete transcript or transcripts of pre-professional and professional credits, each bearing the seal of the school of issuance, said transcripts to be forwarded directly to the Board from the school of issuance.

9.05 *Supervision and control over treatment—definitions.* In order to carry out the requirements of M.S.A., § 148.65, subd. 2, the terms herein defined shall have the following meanings:

9.051 "Prescription," as used in M.S.A., § 148.65, subd. 2, shall mean a written order signed by a physician duly licensed to practice medicine and surgery in this state directing that the physical therapist administer to the physician's patient a specified course of physical therapy, and containing such other orders, directions, and information, as the physician may deem necessary, to inform the physical therapist of the nature and extent of the treatment.

9.052 "Direct supervision" within the meaning of M.S.A., § 148.65, subd. 2, shall mean:

9.0521 a course of physical therapy under prescription, as defined in the foregoing paragraph, administered to a patient by a physical therapist employed by a physician or medical facility approved by the Board;

9.0522 examination, during the course of prescribed physical therapy, by a physician at such times and in such manner as the physician shall deem necessary to insure such change in the course of treatment as may be indicated;

9.0523 a registered physical therapist shall not, without the express direction of a physician duly licensed to practice medicine and surgery in the State of Minnesota, initiate, change, or terminate treatment; provided, however, in the case of emergency, such rule shall not prohibit a registered therapist from changing or terminating treatment which it appears that the patient cannot tolerate and, provided further, that the attending physician is notified immediately of such action.

9.053 Every registered physical therapist who shall annually renew his registration as required by M.S.A., § 148.73 shall indicate in each renewal, on forms provided by the Board, the name of his then current employer and place of employment.

Rule 10. Regulations Governing the Licensing and Practice of Masseurs and Masseuses

10.01 *Application for Licensure.* An application for admission to a licensing examination to practice massage as provided by M.S.A., § 148.36, shall be filed with the Board as hereinafter prescribed. If the Board finds that the application is complete and that all of the requirements of the statute and of these regulations have been met, it shall advise the applicant of the time, date and place of the examination.

10.02 The application shall be made on forms provided by the Board and shall require the applicant to submit the following information:

10.021 Original or certified copy of birth certificate.

10.022 Original or certified copy of high school diploma, transcript of high school credits, or evidence of equivalent education.

10.023 Original or certified copy of diploma, degree or certificate, or evidence satisfactory to the Board, indicating that the applicant has satisfactorily completed an approved course of training complying with the provisions of M.S.A., § 148.37.

10.024 Evidence, satisfactory to the Board, that the applicant is of good moral character.

10.025 An unmounted recent photograph with the affidavit of the applicant on the reverse side thereof that the photograph is that of the applicant.

10.03 An applicant, prior to registration, shall be examined in the subject matter described in M.S.A., § 148.38, and a listing of the subjects to be covered shall be made available by the Board to the applicant prior to examination. Such examination may be oral, written, or practical, and shall be conducted by the Board with the assistance of such experts as the Board may select, who are skilled in the art and science of massage, and who are duly licensed to practice massage in this state.

10.04 The Board, in its discretion, may issue a license to practice massage in this state without examination to any person holding a license from any other state or foreign country whose requirements for such license, as determined by the Board, are equivalent to those of the State of Minnesota. An applicant for registration without examination shall submit, on forms provided by the Board, the following information:

10.041 Original or certified copy of birth certificate.

10.042 Original or certified copy of high school diploma, transcript of high school credits, or evidence of equivalent education.

10.043 Original or certified copy of diploma, degree or certificate of completion of an approved course in massage.

10.044 Original or certified copy of license or certificate to practice massage issued by the state or country from which the applicant is seeking reciprocal licensure.

10.045 Unmounted recent photograph of applicant with an affidavit on the reverse side thereof made by the applicant that the photograph is that of the applicant.

10.046 Evidence, satisfactory to the Board, that the applicant is of good moral character.

Continued

Rule 11. Regulations Governing Practice of Midwifery

11.01 *Definition of Midwifery:* As used in M.S.A., § 148.30, the practice of midwifery includes the furthering or undertaking by any person to assist or attend a woman in normal pregnancy and childbirth, but shall not include the use of any instrument at a childbirth, except such instrument as is necessary in severing the umbilical cord, nor does it include the assisting of childbirth by any artificial, forcible, or mechanical means, nor the removal of adherent placenta, nor the administering, prescribing, advising, or employing, either before or after any childbirth, of any drug, other than a disinfectant or cathartic.

11.02 An application for admission to a licensing examination to practice midwifery in this state shall be filed with the Board as hereinafter prescribed. If the Board finds that the application is complete and that all of the requirements of the statute and of these regulations have been met, it shall advise the applicant of the date and place of the examination.

11.03 The application shall require the applicant to submit the following information:

11.031 Original or certified copy of high school diploma or evidence of equivalent education.

11.032 Original or certified copy of diploma, degree or certificate, or evidence satisfactory to the Board, indicating that the applicant has satisfactorily completed an approved curriculum in midwifery in an approved school or maternity hospital recognized by the Board.

11.033 Evidence, satisfactory to the Board, that the applicant is of good moral character.

11.034 An unmounted recent photograph with the affidavit of the applicant on the reverse side thereof that the photograph is that of the applicant.

11.04 The examination shall be both oral and written and shall include the following subjects: anatomy of the pelvis and female generative organs; physiology of menstruation; diagnosis and management of pregnancy, fetal presentation and position; mechanism and management of normal labor; management of the puerperium; injuries to the genital organ following labor; sepsis and asepsis in relation to labor; special care of the bed and lying-in room; hygiene of the mother and infant; asphyxiation, convulsions, malformation and infectious diseases of the newborn; cause and effects of ophthalmia neonatorum; abnormal conditions requiring attendance of a physician.

11.05 The Board may revoke or refuse to renew the license of any midwife for unprofessional or dishonorable conduct which shall include but not be limited to the following:

11.051 The conviction of a crime of criminal abortion or crimes involving moral turpitude.

11.052 Neglect or refusal to promptly make proper returns to a health officer or health department of births, of a puerperal, contagious or infectious disease.

11.053 Failure promptly to secure the attendance of a duly licensed physician in case of miscarriage, hemorrhage, abnormal presentation or position, retained placenta, convulsions, prolapse of the cord, fever during parturient stage, inflammation or discharge from the eyes of the newborn infant, or whenever any abnormal or unhealthy symptoms appear either in the mother or infant during pregnancy, labor, or the puerperium.

Rules and Regulations Pertaining to Professional Corporations, Proposed by the Minnesota State Board of Medical Examiners on November 19, 1964, Pursuant to Authority Conferred by Minnesota Statutes Annotated, Sections 319.01 to 319.23, inclusive, and Sections 15.0411-15.0415,, inclusive.

The following rules are adopted to carry out the purpose and intent of M.S.A., §§ 319.01 to 319.23, inclusive.

Rule 12. Regulations Governing Establishment and Operation of Professional Corporations

12.01 *Application for Registration.* A professional corporation organized in accordance with the provisions of M.S.A., §§ 319.01 to 319.23, inclusive, shall, before commencing operation or rendering professional service, make application to the Board for a certificate of registration as hereinafter prescribed. If the Board finds that the application is complete and that all of the requirements of the statute and of these regulations have been met, it shall issue to the applicant a certificate of registration which shall constitute the authority of the professional corporation to commence rendering professional services.

12.02 The application shall be submitted on forms prepared by the Board, which forms shall require the applicant to submit the following information:

12.021 Certified copy of articles of incorporation and by-laws and all existing amendments filed in the office of the Secretary of State.

12.022 The address of the registered office of the corporation and the name of its proposed registered agent, if any, for service of process.

12.023 The name or names and respective addresses of the directors and officers of the corporation.

12.024 In the case of a corporation organized under M.S.A., c. 301, a statement of the aggregate number of issued shares, itemized by classes and the person or persons to whom issued.

12.025 In the case of a corporation organized under M.S.A., c. 317, a statement of the names of the members of the corporation.

12.026 A description of the nature of the professional services and ancillary services, if any, to be provided by the corporation.

12.027 The location or locations of the premises at which the applicant corporation proposes to provide professional services.

12.028 A statement listing the name or names of employees, other than members or shareholders of the corporation, who are licensed under M.S.A., c. 147, to practice medicine and surgery within the State of Minnesota.

12.03 The application shall be executed by the corporation by its president and secretary and shall be forwarded to the Board, together with a registration fee in the amount of One Hundred Dollars ($100.00).

12.04 If the Board finds, upon investigation, that the application conforms to all the requirements of M.S.A., c. 319, and the regulations issued thereunder, the Board shall issue a certificate of registration indicating thereon the establishment or establishments at which said certificate of registration shall authorize the applicant to provide professional services.

12.05 Upon the issuance of a certificate of registration by the Board, the corporation shall be authorized to provide the professional services described in its application.

12.06 *Annual Renewal of Registration.* On or before December 1 of each year, each registered corporation shall submit, on forms provided by the Board, an application for the renewal of its certificate of registration. Such application shall be accompanied by a fee in the amount of Twenty-five Dollars ($25.00). The Board shall require the applicant to submit such information as will permit the Board to determine that the applicant corporation is in compliance with the requirements of M.S.A., §§ 319.01 through 319.23, inclusive, and the regulations issued thereunder.

12.07 *Denial, Suspension or Revocation of Certificate of Registration.* The Board may suspend or revoke any certificate of registration in accordance with the provision of M.S.A., § 319.12, provided, however, that such action shall be taken only after written notice and opportunity for hearing thereon in the manner and in accordance with the procedures adopted by the Board governing the conduct of contested cases.

Continued

12.08 *Change of Location.* A certificate of registration issued hereunder shall be applicable only at the location or locations indicated therein. A corporation desiring to change the location or locations of any establishments to which such certificate of registration is applicable shall, at least sixty (60) days prior to such change of location, file with the Board a notice of intent to change location of registered establishment. Such notice shall include the following information:

12.081 The name of the registered corporation.

12.082 The location or locations for which the current certificate of registration is applicable.

12.083 The proposed new location at which the corporation intends to provide professional services.

12.084 A statement showing the names of the shareholders, members, or employees who will provide professional services at the proposed new location.

The Board shall, after receipt of such notice and approval, issue the certificate of registration applicable to the new location at which the corporation intends to provide professional services.

12.09 *Changes in Shareholders, Members or Licensed Employees of Corporation.* Whenever a professional corporation, organized under M.S.A., c. 319, intends to admit to the corporation a new shareholder, member or licensed employee, the corporation shall, at least thirty (30) days prior thereto, notify the Board of its intended action, indicating thereon the identity, state of current licensure to practice medicine and such other information as the Board may require to permit it to investigate and determine whether such new shareholder, member or licensed employee is qualified to practice medicine in the State of Minnesota.

12.10 *Death or Disqualification of Shareholder or Member.* Each corporation holding a certificate of registration issued under M.S.A., c. 319, shall, in the event of death or disqualification of one of its shareholders, members, or employees licensed under M.S.A., c. 147, notify the Board within thirty (30) days thereafter, and shall, in the case of a shareholder or member, prior to the expiration of ninety (90) days from the date of death or disqualification, advise the Board concerning the transfer or other disposition of the shares of such deceased or disqualified shareholder or member.

Procedural Rules and Regulations Proposed by the Minnesota State Board of Medical Examiners on November 19, 1964, Pursuant to Authority Conferred by Minnesota Statutes Annotated, Sections 15.0411-15.0415, inclusive.

The following procedural rules are adopted to carry out the purpose and intent of M.S.A., §§ 15.0411-15.0415, inclusive, and govern the conduct of all proceedings defined as a contested case within the meaning of M.S.A., § 15.0411, subd. 4.

Rule 13. Procedural Rules

13.01 *Definitions.* For the purposes of these rules, the terms defined in this section have the following meanings:

13.011 "Board" means the Minnesota State Board of Medical Examiners or any member or members thereof authorized by law to adjudicate contested cases.

13.012 "Contested Case" means a proceeding before the Board in which the legal rights, duties or privileges of specific parties under the provisions of any statute granting jurisdiction to the Board are required by law or constitutional right to be determined after a Board hearing.

13.013 "Party" includes the Board, the respondent, and any person, other than a member of the Board in his official capacity, who has been permitted to appear in the proceeding.

13.014 "Respondent" means any person or professional corporation against whom an accusation or charge has been filed pursuant to any statute granting jurisdiction to the Board, or any person or professional corporation which is subject to a dispute concerning any legal rights, duties or privileges granted or conferred thereby.

13.02 *Revocation, Suspension, etc.* A hearing to determine whether a right, license or privilege should be revoked, suspended, limited or conditioned, shall be initiated by filing an accusation. The accusation shall be a written statement of charges which shall set forth in ordinary and concise language the acts or omissions with which the respondent is charged and shall be in sufficient detail to enable the respondent to prepare his defense. It shall specify the statutes and rules which the respondent is alleged to have violated, but shall not consist merely of charges phrased in the language of such statutes and rules. The accusation shall be verified by a member of the Board. The verification may be on information and belief.

13.03 *Hearing on Issuance or Renewal of License.* A hearing to determine whether a right, license or privilege should be granted, issued or renewed shall be initiated either by the Board or by the applicant by filing a statement of issues. The statement of issues shall be a written statement specifying the statutes and rules with which the applicant must show compliance by producing proof at the hearing and, in addition, any additional matters which have come to the attention of the initiating party and which would bear upon the issues presented. The statement of issues shall be verified by the initiating party. The verification may be on information and belief. If the Board is the initiating party, the statement of issues shall be served in the same manner as an accusation. If the applicant is the initiating party, the statement of issues shall be served on the Board by registered or certified mail, addressed to the Board at 230 Lowry Medical Arts Building, Saint Paul, Minnesota, 55102. If the initiating party is the Board, the applicant may request a hearing in the manner provided in Rule 13.05 hereof. If the initiating party is the applicant, the statement of issues shall be considered as a request for hearing, and a hearing shall be granted to applicant within thirty (30) days after service upon the Board of the statement of issues.

13.04 *Service of Accusation; Request for Hearing; Form, Manner and Proof.*

13.041 Upon the filing of the accusation, the Board shall serve a copy thereof on the respondent as provided in 13.043 hereof. In addition to the matters to be included in the accusation as set forth in 13.02 hereof, the Board may include with the accusation any additional information which it deems appropriate. The copy of the accusation shall include or be accompanied by the statement that respondent may request a hearing by notifying the Board thereof within fifteen (15) days after service upon him of the accusation, and that failure to do so will constitute a waiver of his right to a hearing.

13.042 The statement to respondent shall be substantially in the following form:

> Unless a written request for a hearing, signed by you or on your behalf is delivered or mailed to the Minnesota State Board of Medical Examiners at 230 Lowry Medical Arts Building, Saint Paul, Minnesota, 55102, within fifteen (15) days after the accusation was personally served on you or mailed to you, the Minnesota State Board of Medical Examiners may proceed upon the accusation without a hearing.

13.043 If the respondent is a resident of the State of Minnesota and can be found therein, the accusation and all accompanying information shall be served upon respondent personally in the manner provided by law for the service of a summons in a civil action. If the respondent is not a resident of the State of Minnesota, or if the respondent is a resident of the State of Minnesota but cannot be found therein, the accusation and all accompanying information shall be served upon respondent by registered or certified mail, addressed to the most recent address theretofore furnished by the respondent to the Board, and the same shall be deemed received by respondent five (5) days after having been deposited in the United States mail, post-

Continued

age prepaid, addressed to such address. The filing by respondent of a request for hearing or his appearance in the proceeding shall constitute a waiver of any defect in such service. Service may be proved by the affidavit of the person making the same.

13.044 Filing of a request for hearing shall be deemed a specific denial of all parts of the accusation not expressly admitted. Failure to file such a request shall constitute a waiver of respondent's right to a hearing, but the Board, in its discretion, may nevertheless grant a hearing.

13.05 *Time and Place of Hearing.* The Board shall determine the time and place of the hearing, which shall be held within thirty (30) days after receipt by the Board of the request for hearing. The hearing shall be held in Saint Paul, Minnesota, at a place designated by the Board, unless the parties, by agreement, select another place within the State of Minnesota.

13.06 *Notice of Hearing.* The Board shall deliver or mail a Notice of Hearing to all parties at least ten (10) days prior to the hearing. The Notice of Hearing to respondent shall be substantially in the following form:

> You are hereby notified that a hearing will be held before the Minnesota State Board of Medical Examiners at (insert place of hearing) on the __ day of __________, 19____, at the hour of ________, ____M., o'clock, upon the charges made in the accusation served upon you. You may be present at the hearing, may be, but need not be, represented by counsel, may present any relevant evidence, and will be given full opportunity to cross-examine all witnesses testifying against you.

13.07 *Depositions for Use as Evidence in the Hearing.* On request of the respondent, or upon notice from the Board to the respondent, the Board may permit the testimony of any material witness, residing within or without the state, to be taken for use as evidence in the hearing, by deposition in the manner prescribed by law for such depositions in civil actions. The request or notice shall set forth the nature of the pending proceedings; the name and address of the witness whose testimony is desired; a showing of the materiality of his testimony; a showing that the witness will be unable to attend; and the Board shall, thereupon, forward a request to the witness to appear and testify before an officer named in the request.

13.08 *Conduct of Hearing.*

13.081 Every hearing in a contested case shall be presided over by a member of the Board. A case may be heard by six (6) or more members of the Board.

13.082 The attorney for the Board shall advise the member or members of the Board concerning the conduct of the hearing and rulings on the admission or exclusion of evidence and other matters of law.

13.083 Any member of the Board shall voluntarily disqualify himself and withdraw from any case in which he cannot accord a fair and impartial hearing or consideration. Any party may request the disqualification of any Board member by filing an affidavit, prior to the taking of evidence at a hearing, stating with particularity the grounds upon which it is claimed that a fair and impartial hearing cannot be accorded. The issue shall be determined by the other members of the Board. No Board member shall withdraw voluntarily or be subject to disqualification if his disqualification would prevent the existence of a quorum qualified to act in a particular case.

13.084 All proceedings at the hearing shall be reported in writing, and the Board shall prepare an official record, which shall include testimony and exhibits in each contested case, but it shall not be necessary to transcribe the record unless requested for purposes of rehearing or court review.

13.09 *Evidence.*

13.091 All evidence shall be taken only on oath or affirmation.

13.092 Each party shall have the right to call and examine witnesses; to introduce exhibits; to cross-examine opposing witnesses on any matter relevant to the issues even though that matter was not covered in direct examination; to impeach any witness regardless of which party first called him to testify; and to rebut the evidence against him. If respondent does not testify in his own behalf, he may be called and examined as if under cross-examination.

13.093 The Board may admit and give probative effect to relevant evidence which possesses probative value and shall not be bound by the technical rules relating to evidence and witnesses; provided, however, that the Board shall give effect to the rules of privilege recognized by law. Hearsay evidence may be used for the purpose of supplementing or explaining any direct evidence but shall not be sufficient in itself to support a finding unless it would be admissible over objection in civil actions. All evidence including records and documents (except tax returns and tax reports) in the possession of the Board of which it desires to avail itself shall be offered and made a part of the record in the case. Documentary evidence may be received in the form of copies or excerpts, or by incorporation by reference.

13.10 *Decision in Contested Case.*

13.101 No right, license or privilege shall be granted, issued, renewed, revoked, suspended, limited or conditioned except upon the affirmative vote of at least six (6) members of the Board.

13.102 Whenever, in a contested case, a member of the Board who has not participated in the hearing votes in the decision of the case, a final decision, if adverse to the respondent, shall not be made until a proposed decision, including the statement of reasons therefor, has been served on the respondent, and opportunity has been afforded to file exceptions and present argument to all of the members of the Board who are to render the final decision.

13.103 The respondent shall have the opportunity to present either oral or written argument and to present additional newly discovered evidence after the close of the record but prior to final decision.

13.104 Informal disposition of a contested case may be made in the manner prescribed by law.

13.11 *Form of decision; findings.* Every decision and order adverse to a party to the proceeding shall be in writing and shall contain a statement of findings or reasons, a determination of the issues presented, and the penalty, if any, or decision of the Board. The findings shall consist of a statement of the conclusions upon each contested issue of fact necessary to the decision. Parties to the proceedings shall be notified of the decision and order in person or by mail. A copy of the decision and order and accompanying statement of reasons together with proof of service shall be delivered or mailed, upon request, to the respondent or to his attorney of record.

13.12 *Effective date of decision; stay of execution; notification of suspension or revocation.*

13.121 The decision or order of the Board shall become effective immediately upon its service on respondent; provided, however, that the Board may, in its discretion, stay the enforcement of its decision pending appeal or reconsideration within thirty (30) days after said service.

13.122 The Board may, upon its own motion or upon petition by respondent, reconsider or grant a rehearing of any decision rendered in a contested case or may condition any such decision upon just and reasonable grounds.

13.123 The filing of a petition for review shall not automatically stay the enforcement of the Board decision.

Reason is the light, the sun, of the brain. It is the compass of the mind, the ever-constant Northern Star, the mountain peak that lifts itself above all clouds.

— Robert Ingersoll

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Perinatal Mortality Study

Severe Anemia in the Newborn*

Case Report

The 29-year-old mother of the infant under study was Group A, Rh positive, and this was her fifth pregnancy. She had had no difficulty during her other four pregnancies; her children are living and well. She had no illness during her present pregnancy; the only drugs she received were prenatal iron, calcium, and vitamin D capsules twice daily. About two to three days prior to labor at 38 weeks she felt something was wrong with the infant because fetal movements were markedly decreased. Rupture of the membranes occurred 28 hours prior to delivery, and labor lasted 11½ hours. A large bloody show occurred 30 minutes before delivery. The delivery was spontaneous ROA under pudendal block anesthesia. The placenta measured 18 cm. in diameter, weighed 420 grams, and 1/6 of the maternal surface was covered with a thick tenaceous mass of clotted blood indicating abruptio placenta.

At birth the male infant was pale and flaccid and weighed five pounds, 11 ounces. The respirations were gasping. There was no petechia or jaundice. The cord hemoglobin was reported 45 minutes after birth as 4.6 grams %, and the white blood count 30,750 per mm^3. with a differential of 63% diff. pmn., 6% stab., 1% immature cells, 27% lymph., 1% mono., and 2% eos. The mother's hemoglobin was 13.5 grams %. No tests were done to detect fetal hemoglobin in the mother's blood. The infant was given oxygen in an incubator. At one and one-half hours of age a pediatrician was called to see the infant, and he recommended that the child be sent to another hospital for care. At two hours of age the infant arrived at the second hospital. He was pale and gray-appearing; his respirations were 14 to 16 per minute and irregular; his heart rate was 100 per minute and regular; his hemoglobin, 4.2 grams %, hematocrit 17%. It was then decided to give him an emergency transfusion of fresh Group O, Rh negative blood. The umbilical vein was catheterized, and the venous pressure was less than 2 cm. of water. Fifty-eight cc. of whole blood was rapidly given, and the infant suddenly expired at four hours of age.

Autopsy revealed the infant to be pale and cyanotic with no jaundice present. The lungs showed massive atelectasis, and many of the alveoli were filled with epithelial squames, interpreted by the pathologist as evidence of intrauterine respiratory efforts. The heart, liver, spleen, adrenals, kidneys, and brain showed no petechiae and were found to be normal.

Comment

This case demonstrates anemia in the newborn and hemorrhage from the placenta associated with an abruptio placenta. The Ramsey County Perinatal Mortality Study Committee feels that the infant should have received emergency blood at 45 minutes of age when the cord hemoglobin was reported as 4.6 grams %, rather than after transfer to another hospital when the child was almost four hours of age. Blood should be given carefully, with constant monitoring of the venous pressure.

Discussion

Kendall[1] lists the following causes of anemia in the newborn infant:

"1. Blood group incompatibility
2. Hemorrhage from the placenta
3. Hemorrhage into or from the umbilical cord
4. Hemorrhage into body organs
5. Infections
6. Fetomaternal transfusion
7. Hemorrhage from one twin to another"

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*Ramsey County Perinatal Mortality Study Committee.

Continued

Schaffer[2] states, "When anemia is the only or is the major presenting symptom at birth, its cause is apt to be found in excessive hemolysis or fetal hemorrhage. The anemia of infection is overshadowed by associated symptoms, since those infections which have been severe enough to produce serious anemia by the time of birth almost always have led to purpura, jaundice, hepatosplenomegaly and other signs. In the infant pale at birth one first searches for evidences of hemolytic disease (Coombs tests, direct and indirect, erythroblastosis, normoblastosis and reticulocytosis, urebilinuria and excessive urobilinogen in stools) and for its possible causes (Rh, ABO or other incompatibilities, circulation antibodies, red-cell or hemoglobin defects). We might repeat here once again that this search must be delayed if anemia is severe, until blood replacement and digitalis therapy shall have been accomplished, so that the heart will not fail while one is looking for causes. The bilirubin content of the blood probably will be found elevated during the first day if the disorder is hemolytic, but it need not be very high, and the liver and spleen are almost always enlarged.

"If no evidence of or causes for hemolysis can be found, one may entertain the considerably less common diagnosis of posthemorrhagic anemia. This may be difficult to prove. A history of maternal bleeding of unusual quantity or of unusually bright red color before or during delivery is significant. Also the presence of placenta previa or the history of delivery by cesarean section can be considered suggestive evidence in favor of fetal bleeding. The coincidental delivery of an identical twin supplies a possible locus where blood loss may have occurred. If all these have been lacking, one searches for evidence that fetal blood has entered the maternal blood stream.

"The posthemorrhagic anemic newborn is pale and may be shocked, but he is not apneic and his heart rate is more apt to be unduly rapid than unduly slow. The liver and spleen are not enlarged, nor are there any evidences of bleeding into the skin or elsewhere."

Summary

A case of severe anemia in the newborn and hemorrhage from the placenta associated with an abruptio placenta is presented, and the differential diagnosis of anemia in the newborn infant is discussed.

The Ramsey County Perinatal Mortality Study Committee feels that all infants with severe anemia at birth should receive immediate blood transfusion or exchange transfusion of fresh Group O, Rh negative compatible blood. This can be done through the umbilical vein. With life-threatening, severe anemia, sometimes it is necessary to give blood before the complete etiologic factors responsible for the anemia can be determined.

References

1. Kendall, Norman: Anemia in the Newborn Infant. Pediat Clin N Amer 10:613, 1963.
2. Schaffer, Alexander: Differential Diagnosis of Anemia in the Newborn, Diseases of the Newborn. W. B. Saunders Company, Philadelphia, 1960.

The meek may inherit the earth, but they'll cease being meek as soon as they come into their inheritance.

Special Article

Cervical Cytology Survey

SAMUEL A. SMITH, M.D.*
Minneapolis, Minnesota

IT HAS often been said that not enough is being done to encourage the use of the pap smear as a routine test for cervical cancer. It is well known that, since its introduction some thirty years ago, acceptance has been slow. As the use of the smear as a routine diagnostic procedure has increased, however, the morbidity and mortality from cancer of the cervix has decreased. For example, the death rate in Minnesota was 40.0 per 1,000 in 1944 and 29.9 per 1,000 in 1963.

In the light of a growing awareness of the effectiveness of the smear, and the concern that more ought to be done to promote its routine use, it was decided to survey Minnesota physicians on the subject. It was anticipated that the results of the survey would encourage and increase the use of this diagnostic procedure.

Materials and Methods

The questionnaire and accompanying explanatory letter (Fig. 1) were developed.** The questionnaire was designed to separate responders into groups characterized by type of practice and routine use of the smear. It was arbitrarily decided to poll only obstetrician-gynecologists, internists, general practitioners, and general surgeons. A fifth category, "other," includes physicians who stated that they are in institutional or industrial medicine. As the initial questionnaires were returned, those indicating a type of practice other than the designated ones were eliminated.

Results

There were finally eighteen hundred thirty-five questionnaires completed and returned by physicians in the specified categories (Table 1). One thousand six hundred eighty-four physicians, or 91.8% of the responders

TABLE I
Analysis of Response to Questionnaire

Mailing Number 1	
Completed for survey	1,500
Doctor deceased	10
Doctor left state	13
Doctor retired	43
Eliminated by type of practice	500
Not returned	1,019
Total	3,085
Mailing Number 2	
Completed for survey	335
Doctor deceased	6
Doctor left state	9
Doctor retired	16
Eliminated by type of practice	59
Not returned	244
Total	669

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*Cancer Control Officer, U. S. Public Health Service assigned to Minnesota Department of Health, Minneapolis, Minnesota.

**The Cancer Control Section of the Minnesota Department of Health; the Cancer Committee of the Minnesota State Medical Association, and the Cytology Committee, Minnesota Division, American Cancer Society.

Continued

state that they examine and/or treat female pelvic complaints. It is this group of 1,684 physicians that this paper is concerned with. The lone gynecologist who reported that he did not examine or treat pelvic complaints stated that he acted only as a consultant; he did not complete the questionnaire (Table 2).

Use of the Smear as a Routine Test

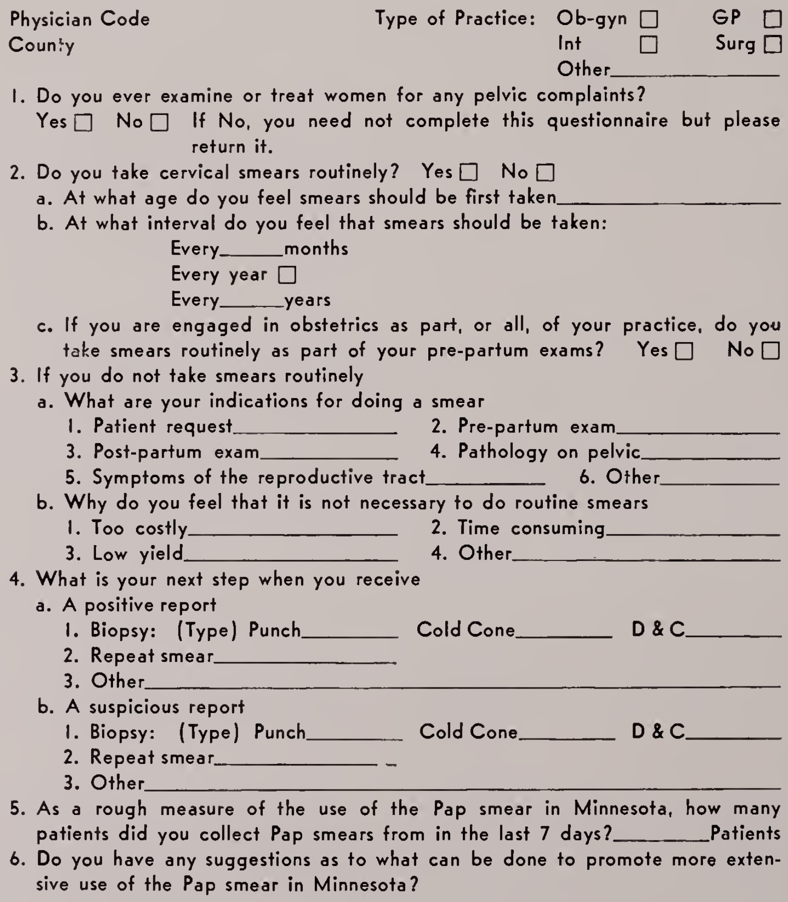
One thousand two hundred and twenty-three physicians (72.6%) of the responders (1,684) who handle pelvic complaints state that they take routine pap smears. In this group are 93.1 per cent of the obstetrician-gynecologists, 67.0 per cent of the general practitioners, 89.8 per cent of the internists, and 72.2 per cent of the surgeons. It appears then that a significant number of those physicians who handle pelvic complaints take routine smears. Further questioning of these physicians reveals that 64.3 per cent of them feel that the first smear should be taken prior to age thirty; this group includes 73.2 per cent of the obstetrician-gynecologists and 65.6 per cent of the general practitioners. The earliest suggested age was 13 (Tables 3 and 4).

Frequency of Taking Smears

Eighty per cent of each group advocate taking smears once a year (Table 5).

Use of the Smear as a Part of the Pre-partum Examination

The final question asked of those doing smears on a routine basis concerned use of the smear as part of the pre-partum examination. It has been advocated that the smear be a part of this examination since expectant mothers are a captive group. Four hundred twenty-five (34.8%) of those responding to this question (1,223) state that it is part of



Physician Code
County

Type of Practice: Ob-gyn ☐ GP ☐
Int ☐ Surg ☐
Other____________

1. Do you ever examine or treat women for any pelvic complaints?
   Yes ☐ No ☐ If No, you need not complete this questionnaire but please return it.
2. Do you take cervical smears routinely? Yes ☐ No ☐
   a. At what age do you feel smears should be first taken____________
   b. At what interval do you feel that smears should be taken:
      Every______months
      Every year ☐
      Every______years
   c. If you are engaged in obstetrics as part, or all, of your practice, do you take smears routinely as part of your pre-partum exams? Yes ☐ No ☐
3. If you do not take smears routinely
   a. What are your indications for doing a smear
      1. Patient request____________ 2. Pre-partum exam____________
      3. Post-partum exam____________ 4. Pathology on pelvic____________
      5. Symptoms of the reproductive tract__________ 6. Other__________
   b. Why do you feel that it is not necessary to do routine smears
      1. Too costly____________ 2. Time consuming____________
      3. Low yield____________ 4. Other____________
4. What is your next step when you receive
   a. A positive report
      1. Biopsy: (Type) Punch________ Cold Cone________ D & C________
      2. Repeat smear____________
      3. Other____________________________________
   b. A suspicious report
      1. Biopsy: (Type) Punch________ Cold Cone________ D & C________
      2. Repeat smear____________
      3. Other____________________________________
5. As a rough measure of the use of the Pap smear in Minnesota, how many patients did you collect Pap smears from in the last 7 days?________Patients
6. Do you have any suggestions as to what can be done to promote more extensive use of the Pap smear in Minnesota?

Fig. 1

TABLE 2
Analysis of Responders by Type of Practice and Care of Female Complaints

Type of Practice	Total Group Number	Total Group Percent	Examines and/or Treats Females Number	Examines and/or Treats Females Percent	Does Not Examine or Treat Females Number	Does Not Examine or Treat Females Percent
Obstetrics and Gynecology	145	7.9	144	99.3	1	0.7
Internist	267	14.6	225	84.3	43	15.7
General Practice	1,139	62.0	1,099	96.5	38	3.5
Surgery	223	12.2	158	70.9	66	29.1
Other	61	3.3	58	95.1	3	4.9
Total Group	1,835	100.0	1,684	91.8	151	8.2

TABLE 3
Type of Practice: Routine Use of Pap Smears

	Examines and/or Treats Females Number	Routine Pap Smears Number	Routine Pap Smears Percent	No Routine Pap Smears Number	No Routine Pap Smears Percent
Obstetrics and Gynecology	144	134	93.1	10	6.9
Internist	225	202	89.8	23	10.2
General Practice	1,099	736	67.0	363	33.0
Surgeons	158	114	72.2	44	27.8
Other	58	37	63.8	21	36.2
Total Group	1.684	1,223	72.6	461	27.4

TABLE 4
Analysis, by Type of Practice, of Suggested Age of First Smear

Age Group	Entire Group Number	Entire Group Percent	Ob.-Gyn. Number	Ob.-Gyn. Percent	Internist Number	Internist Percent	General Practice Number	General Practice Percent	Surgeon Number	Surgeon Percent	Other Number	Other Percent
10–14	14	1.1	2	1.5	3	1.5	6	0.8	1	0.9	2	5.4
15–19	180	14.7	25	18.7	28	13.9	114	15.5	11	9.7	2	5.4
20–24	387	31.7	52	38.8	63	31.2	235	31.9	25	21.9	12	32.4
25–29	206	16.8	19	14.2	30	14.9	128	17.4	25	21.9	4	10.8
30–34	192	15.7	10	7.5	39	19.3	114	15.5	22	19.3	7	18.9
35–39	79	6.5	2	1.5	12	5.9	53	7.2	8	7.0	4	10.9
40+	38	3.1	1	0.7	6	2.9	19	2.6	9	7.9	3	8.1
Not Stated	127	10.4	23	17.1	21	10.4	67	9.1	13	11.4	3	8.1
Total	1,223	100.0	134	100.0	202	100.0	736	100.0	114	100.0	37	100.0

TABLE 5
Frequency of Doing Smear by Type of Practice

Frequency of Taking Smear	Ob.-Gyn. Number	Ob.-Gyn. Percent	Internist Number	Internist Percent	General Practice Number	General Practice Percent	Surgeon Number	Surgeon Percent	Other Number	Other Percent	Totals Number	Totals Percent
More than once per year	3	2.2	3	1.5	40	5.4	7	6.2	6	16.2	59	4.8
Once per year	116	86.6	175	86.6	609	82.8	96	84.2	25	67.6	1,021	83.5
Less than once per year	13	9.7	20	9.9	78	10.6	8	7.0	4	10.8	123	10.1
No Response	2	1.5	4	2.0	9	1.2	3	2.6	2	5.4	20	1.6

Continued

their examination. It was assumed that no response to this question meant that the physician did not engage in obstetrics as part or all of his practice (Table 6).

Indications for Doing a Pap Smear

Those physicians who state that they did not take routine pap smears were questioned concerning their reasons for doing any smear at all. The choices were patient request, pathology on pelvic examination, symptoms of the genitourinary tract and pre and post-partum examination (Table 7). It is evident that patient request plays a significant role among these physicians, and the smear is often used as a primary diagnostic tool rather than as a screening device. One hundred per cent of the physicians in this group had two or more responses to this question.

Reasons for Not Doing Routine Smears

In this case the responders were given a choice of responses. The results are tabulated with respect to the frequency of response. It is evident (Table 8) that cost and low yield are major factors influencing this group in its decision not to do routine smears. According to statements made by many responders, the cost depends largely on the fee charged by the laboratories processing the smears. The suggestion was often made that the state establish a laboratory to process smears free or at cost.

What Do You Do When you Receive Other Than a Negative Report

The entire group of responders were asked what they did when they received a suspicious or positive report. The choice of response was any combination of biopsy (punch, cold cone, D and C), repeat smear, other. More than 90 per cent of the "other" was filled in by referral. The responses indicate a large combination of possible procedures (Table 9). It is evident from the responses that the majority of physicians answering this question favor repeating the smear.

Responders were then asked what their next step would be if they received a positive report. Again any combination of the choices was accepted, and as in the previous question there was a great number of possible combinations (Table 10).

Number of Smears Being Done

In an attempt to ascertain how many smears are being done in Minnesota each responder was asked to state how many smears he had done in the seven-day period

TABLE 6
Use of Pap Smear in Pre-partum Examination

	Ob.-Gyn.		Internist		General Practice		Surgeon		Other		Totals	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Yes	70	52.2	1	0.5	336	45.7	9	7.9	9	24.3	425	34.8
No	58	43.3	15	7.4	332	45.1	16	14.0	16	43.2	437	35.7
No Response	6	4.5	186	92.1	68	9.2	89	78.1	12	32.5	361	29.5

TABLE 7
Frequency of Indications for Doing Pap Smears in Those Physicians
Who do not do Routine Pap Smears

Type of Practice	Patient Request	Pathology on Pelvic	Symptoms of Reproductive Tract	Post-partum Examination	Pre-partum Examination
Obstetrics-Gynecology	90.0%	90.0%	70.0%	10.0%	10.0%
Internist	80.0	72.0	64.0	4.0	0.0
General Practice	82.0	79.5	62.6	16.1	7.9
Surgeon	68.6	70.6	47.1	0.0	2.0
Other	76.2	66.7	61.9	0.0	4.8
Total Group	80.3	77.8	61.1	12.9	6.6

TABLE 8
Reasons For Not Doing Routine Pap Smear

Type of Practice	Cost	Low Yield	Takes Too Much Time
Obstetrics-Gynecology	50.0%	50.0%	0.0%
Internist	39.1	56.5	8.7
General Practice	58.7	42.1	7.2
Surgeon	45.5	47.7	4.7
Other	38.1	19.0	9.5
Total Group	55.3	42.5	6.9

TABLE 9
Next Step With Suspicious Report

Total Group		Obstetrics-Gynecology		Internist	
Repeat Smear	56.8%	Repeat Smear	51.4%	Other (referral)	42.9%
		Cold Cone + D+C	15.3%	Repeat Smear	37.9%
		Cold Cone	13.9%		80.8%
			80.6%		
General Practice		**Surgeon**		**Other**	
Repeat Smear	63.4%	Repeat Smear	49.0%	Repeat Smear	39.7%
		Other (referral)	15.3%	Other (referral)	25.9%
		Cold Cone + D+C	10.2%		65.6%
			74.5%		

TABLE 10
Next Step After Receiving a Positive Report

Total Group		Obstetrics-Gynecology		Internist	
Cold Cone	21.1%	Cold Cone + D+C	38.9%	Other (referral)	58.2%
Cold Cone + D+C	21.0%	Cold Cone	31.9%	Repeat Smear	11.9%
Punch + D+C	15.0%		70.8%		70.1%
Repeat Smear	12.3%				
	69.4%				
General Practice		**Surgeon**		**Other**	
D+C	24.8%	Cold Cone + D+C	27.4%	Other (referral)	36.2%
Cold Cone + D+C	23.8%	Cold Cone	22.3%	Cold Cone + D+C	12.1%
Repeat Smear	14.6%	Referral (other)	19.1%	Cold Cone	12.1%
	63.2%		68.8%		60.4%

TABLE 11
Total Physicians Examining and/or Treating Female Pelvic Complaints — 1,684
Total Number of Smears Reported Done in a Seven-day Period — 11,218
Average Number of Smears Per Physician in the Seven-day Period — 6.7

	Obstetrics and Gynecology	Internists	General Practice	Surgeon	Other
Number of Responders	145	267	1,139	223	61
Number of Smears	2,947	1,330	6,014	590	337
Average Number of Smears	20.3	5.0	5.3	2.6	5.5

Continued

prior to receiving the questionnaire (Table 11).

Suggestions Regarding Improving the Pap Smear Program in Minnesota

Each responder was asked to make suggestions for improving the program. One hundred and fifty-one responders did not answer this question. Sixty-nine per cent (69.0%) of those responding suggest an expanded educational program aimed at both physicians and the laity. Other significant suggestions include: state subsidy for processing smears, and establishment of a state laboratory to do the processing for a nominal fee or free of charge. Frequent protests were made that there is no standard fee for smears, and fees from three to twelve dollars were quoted.

Conclusion

It would appear that this survey was fairly successful. It is quite evident from the responses that a fair number of Minnesota physicians whose practice involves handling of the female genital tract are aware of the usefulness of the smear. It would appear that they also recognize the need for an expanded effort to make this test available to more females in the state.

Requirements for Medical Degrees at Salernum

Candidates were required to be twenty-one years of age, and to produce proofs of having studied Medicine for seven years. As yet the degree thus obtained did not authorize one to practice indiscriminately in every department; for, if the candidate desired to be admitted to practice Surgery, it was required in addition that he should study Anatomy for one whole year. But every one, to whatever degree admitted, must first swear to be true and obedient to the Society of Physicians — to refuse all fees from the poor, *and to have no share of gains with apothecaries.* A book was then put into his hands — a ring upon his finger — his head was crowned with laurel, and he was dismissed with a kiss. (John Ordronaux)*

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*Rapport, Samuel, and Wright, Helen: Great Adventures in Medicine. The Dial Press, New York, 1952, p. 75.

The Laryngoscope

Senor Manuel Garcia (1805-1906), who created the laryngoscope, was a singing-master who wanted to see how his larynx worked. The idea came to him out of a blue sky. With two mirrors it is possible to see round a corner, and the larynx is so far round a corner as to be normally invisible. Garcia bought his two mirrors, a little dental mirror with a long handle, which cost 6 francs, and a hand mirror. The dental mirror he placed firmly against his uvula, and what appeared there he saw in the hand mirror, which reflected a ray of light on to the dental mirror.*

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*Massengill, S. E., M.D.: Sketch of Medicine and Pharmacy. S. E. Massengill Co., Bristol, Tenn.-Va., p. 110.

Some media operations, like some politicians, some clergymen, some labor leaders, some economists, are overly sensitive to the side on which their bread is buttered.
—Leo Rosten

Be humble or you'll stumble. — Dwight L. Moody

Harvey Cushing

(1869-1939)

It has been affirmed by many that the mantle of John Hunter fell upon Harvey Cushing, a life-long exponent of the experimental method. In the domain of neurological surgery, from the earliest mention of trephanning in the time of Hippocrates, to Galen, the first experimental neurologist, and following Ferrier's demonstration of the theory of cerebral localization in 1881, a great volume of experimental research on the brain and spinal cord was done. However, neurosurgery, as a specialty, was not born until the beginning of the present century. ". . . and it is unique in that it was largely the creation of two individuals . . . Sir Victor Horsley laid its foundations, and Harvey Cushing built the edifice of special technique and knowledge that today stands as one of the notable achievements of modern surgery."[1]

Born in Cleveland, of New England stock, from a family of distinguished doctors, Cushing studied at Yale and Harvard. After graduation he applied for a residency in Surgery at Johns Hopkins under Doctor William S. Halsted, which post he held for four years. After a year's study with Theodore Kocher and Hugo Kronecker in Berne, Switzerland, where he did his first work in experimental neurology, he returned to Johns Hopkins. He proposed to Doctor Halsted that he enter the field of neurology. His early mortality rate was extremely high. With utmost diligence and thoroughness, surmounting most of his operative difficulties, ". . .* he developed the method of precise localizing diagnosis for brain tumors and worked out the highly specialized technique for operating upon the brain. . . . The general principles of surgical technique that formed the basis of Cushing's methods were those of his great chief, Halsted . . . Cushing applied these principles to brain surgery with great skill. He controlled bleeding from the scalp by placing a tourniquet around it. For tumors of the sub-occipital region he devised the so-called cross-bow incision which has been the standard one ever since. . . . He introduced the practice of keeping a running record of the patient's blood pressure during the whole course of the operation in order to detect the development of shock — a practice which has since been adopted in all types of surgery. An amusing anecdote is told of Cushing's trials in the early days when he was introducing the blood pressure apparatus in the operating room. At a crucial point during one of his operations the patient showed signs of collapse and he ordered one of the nurses to get the blood pressure machine and find out what the pressure was. It was the custom to apply the apparatus to the patient's leg in those days. There was a long delay during which Cushing, absorbed as he was with difficulties in the operative field, had no time to pay attention to anything

Continued

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*From "The Story of John Hopkins" by Bertram M. Bernheim. McGraw-Hill Book Company. Used by permission.

else. Finally, he felt some encumbrance on one of his own legs and looking down found that the eager nurse had applied the apparatus to his leg rather than to the patient's."[2]

Cushing began to use experimental animal surgery early in his work at Johns Hopkins. By 1904 he was given a building. Doctor William H. Welch suggested that it be named after John Hunter, so it became the Hunterian Laboratory for Experimental Medicine and Surgery. From the day it opened . . . "the S.P.C.A. began camping on its trail. Frequently they slowed up the work — occasionally they stopped it completely — but it was never longer than a week, and efforts to close the laboratory permanently failed dismally. . . . From the beginning Cushing was extremely solicitous of the animals and impressed everyone that there would be no tolerance of cruelty or careless handling. All work was to be done on the highest scientific plane, and nothing should be done without proper and adequate anesthesia; problems had to have sense and reason; they all were to be properly supervised. . ."[3]

One of Cushing's former students who worked with him in the laboratory delineates him: "Among the many men who came to the Hopkins, achieved greatness and shed glamour and renown on the institution, Harvey Cushing must take high rank. . . . The world was his horizon, and properly so, because he was a many-sided man with an intellect of surprising quality. Greatness was literally written all over him — Consider this man . . . — thin, medium-sized, muscular, chiseled features, snapping eyes, quick-thinking, quick-acting, short-tempered, nervous, charming, sarcastic, inconsiderate, impatient, ruthless (depending on changing moods), jealous, lovable, selfish, domineering, demanding — he had a penetrating mind, stupendous ability, and there was nothing he couldn't do and do well once he decided to have a go at it."[4]

During those early years in Baltimore Cushing became close friends with William Osler, his next-door neighbor. From Osler he acquired his love of books, becoming a leading medical bibliophile. After Osler's death, Lady Osler selected Cushing to write her husband's biography. THE LIFE OF SIR WILLIAM OSLER, written in a reverent and masterly hand, is considered the outstanding medical biography of our time. This two-volume work won for Cushing the Pulitzer prize in 1926.

In 1912 Cushing was called to Harvard as Mosley professor of Surgery, and Surgeon-in-Chief to the newly constructed Peter Bent Brigham Hospital. During the next twenty years he accomplished his major work there, where his clinic for neurosurgery attained world renown. "He perfected his methods, accumulated a great mass of data concerning brain tumors, and trained a succession of young men who carried his teachings abroad and established neurosurgery as a speciality in the chief centers of medical education everywhere."[5]

Cushing gave nearly four years of service during World War I, serving first with a Harvard Unit. He organized and directed one of the base hospital units, and served as operating surgeon with the B.E.F. He was transferred to the Medical Headquarters of the A.E.F. as senior consultant in neurosurgery. With unsparing devotion to his work, he was sometimes on duty for sixteen hours at a stretch. This undoubtedly undermined his health for the rest of his life. His daily diary, FROM A SURGEON'S JOURNAL, was printed in book form. It is as vivid and informative as any contemporary document of the period. Three countries awarded him for his great work; the United States by the award of a Distinguished Service Medal, Great Britain by the Order of the Companion of the Bath, and France with the position, Officer of the Legion of Honor.

When Cushing retired from Harvard in 1932, he summarized his work in a monograph entitled, INTRACRANIAL TUMORS, NOTES UPON A SERIES OF TWO THOUSAND VERIFIED CASES WITH SURGICAL MORTALITY PERCENTAGES PERTAINING THERETO. He also wrote a series of articles and monographs on special forms of brain tumors. His short essays are considered gems of modern prose. Inspired by Osler, he became interested in Vesalius, continuing for forty years to collect everything available about him. He corresponded with many Vesalian scholars in this country and Europe. He spent the last years of his life assembling material for a Vesalian bibliography. A BIO-BIOGRAPHY OF ANDREAS VESALIUS was published posthumously.

Cushing's last post was at Yale, where he was Sterling Professor of Neurology, following which he became Emeritus Professor and Director of Studies in the History of Medicine. He donated to Yale his incomparable collection of books and manuscripts, including his Brain Tumor Registry. The historical division of the Yale Library is now the Cushing Library.

Cushing passed away in 1939 at the age of seventy. His pupils are carrying on brilliantly the work he originated. Some have formed a society which bears his name. Although numerous honors, awards and citations came to Cushing, those who knew him well say he would have liked best to have it said about him that he followed the highest tradition of our profession — that he never neglected anything that could bring comfort or benefit to a patient.

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5. Haagensen, p. 324.

Doyle's Austerity

Sir Arthur Conan Doyle started in practice at Southsea with an empty villa, 4 pounds worth of second-hand furniture, a stock of drugs obtained on credit and 2 pounds cash. He found that he could live 'quite easily and well on less than a shilling a day.' Bread, bacon and tea were his staples, with an occasional saveloy. His young brother joined him to perform some of the chores and one day was able to record, 'We have vaxenated a baby and got hold of a man with consumption.' They also got hold of a man with epilepsy, whose fits kept them in butter and tea. 'Poor fellow,' writes Sir Arthur, 'he could never have realized the mixed feelings with which I received the news of a fresh outbreak.'*

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*Turner, E. S.: Call the Doctor. St. Martin's Press Inc., New York, 1959, p. 216.

Kindness — a language which the dumb can speak and the deaf can understand.
— C. N. Bovee

Of 425 patients with confirmed G.I. infections... 387 or 91.1% were treated successfully with Signemycin®

Note:
Loughlin and co-workers* achieved cure (absence of parasites) in all 100 of their patients with *chronic amebic colitis*. Feces became negative in all within the planned ten-day period of Signemycin administration. Upon re-examination of the feces six weeks later, the offending pathogen *(E. histolytica)* had reappeared in only 7 cases.

*Loughlin, E. H. et al.: Antibiot. Med. 7:739, Dec., 1960.

Condition	No. of Patients	No. Responded to Signemycin
Amebiasis	237	222
Cholecystitis and cholangitis	105	97
Enteritis	41	31
Peritonitis	15	14
Various, including pancreatitis, appendicitis and colitis	27	23
Totals	425	387 (91.1%)

consistently effective...often when others fail

Signemycin®

tetracycline HCl, 167 mg.; oleandomycin as triacetyloleandomycin, 83 mg. capsules (250 mg.)

Also available as Syrup, Pediatric Drops, and half-strength Capsules

Brief Summary and Bibliography follow.

Science for the world's well-being® Pfizer *Since 1849*

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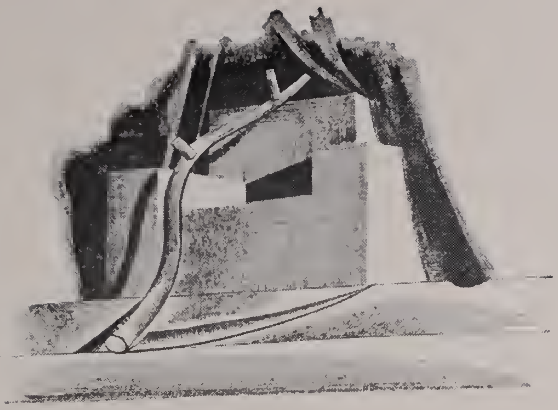

In Memoriam

Death is the crown of life. Were death denied, poor man would live in vain; to live would not be life; even fools would wish to die. — Young

JOHN LOWELL STENNES

Dr. John L. Stennes, 47, Minneapolis physician, died December 10th. He was born at Haynes, North Dakota, and studied at Concordia College at Moorhead, Minnesota, the University of North Dakota and Washington University in St. Louis, Missouri.

Dr. Stennes was a former chief of staff at Swedish Hospital in Minneapolis. He was a member of the Hennepin County Medical Society, Minnesota State Medical Association and American Medical Association.

He is survived by his wife, a son and a daughter.

DAVID KADESKY

Dr. David Kadesky, former St. Paul physician, died December 5th in San Francisco. Dr. Kadesky practiced in the Hamm building in St. Paul. He is survived by his wife.

JOHN E. POWER

Dr. John E. Power, 73, retired Duluth physician, died December 18th after a long illness. A native of London, Ontario, Dr. Power was a graduate of Queens University Medical School, Kingston, Ontario.

He was a past chief of staff of St. Mary's hospital, a fellow of the American College of Surgeons, a member of the St. Louis Medical Society and American Medical Association, and a life member of the Minnesota State Medical Association.

He is survived by his wife and three sons, one of whom is Dr. John E. Power, Jr. of Duluth.

AXEL S. N. NORAN

Dr. Axel Noran, 77, Edina pediatrician, died December 27th. He was born at Fergus Falls, Minnesota, and received his degree of medicine from Northwestern University at Chicago.

He was a member of the Hennepin County Medical Society and American Medical Association. Dr. Noran was a 50 Club member of the Minnesota State Medical Association.

He is survived by his son, Dr. Harold H. Noran of Edina.

RICHARD F. KLINE

Dr. Richard F. Kline, 40, St. Cloud physician, died December 24th. Born in Grand Rapids, Minnesota, he was a graduate of the University of Minnesota School of Medicine.

Dr. Kline was a member of the Stearns-Benton Medical Society, Minnesota State Medical Association, American Medical Association, American College of Physicians, Association of Minnesota Internists, Sertoma Club and Elks Club.

He is survived by his widow and four children.

EDWARD V. GOLTZ

Dr. Edward V. Goltz, 84, St. Paul physician, died December 9th, after a long illness. He was born at Winona, Minnesota, and obtained his medical education at Northwestern University Medical School.

Dr. Goltz was the first medical director of the St. Paul Red Cross regional blood program and a member of the Minnesota Academy of Medicine, Ramsey County Medical Society, American Medical Association, a fellow of the American College of Physicians and a 50 Club and Life member of the Minnesota Medical Association.

He is survived by his wife, one daughter and three sons, two of whom are Dr. Robert Goltz of Minneapolis and Dr. Neill Goltz of Fargo.

Of 748 patients with confirmed G.U. infections... 684 or 91.4% were treated successfully with Signemycin®

Note:
The efficacy of Signemycin was shown in a study of nongonococcal urethritis involving over 1600 patients.* A comparison of the cure rates of sixteen antibiotic and chemotherapeutic agents revealed that Signemycin had the highest incidence of successful response. One hundred and six patients were treated, of which 82 were followed, with cures in 70.

*Willcox, R. R. and Rosedale, N.: Brit. J. Vener. Dis. 38:19, Mar., 1962.

Condition	No. of Patients	No. Responded to Signemycin
Cystitis	29	25
Pyonephritis	30	28
Pyelocystitis	119	112
Prostatitis	14	13
Gonorrhea	66	64
Lymphogranuloma venereum	96	96
Syphilis	31	31
Urethritis, nonspecific	149	131
Various, including infections seen with impaired urinary flow or lithiasis	214	184
Totals	748	684 (91.4%)

consistently effective...often when others fail

Signemycin®

tetracycline HCl, 167 mg.; oleandomycin as triacetyloleandomycin, 83 mg.

capsules (250 mg.)

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Brief Summary and Bibliography follow.

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The Blue Shield

Excess Payments From Health Insurance

Should a patient be able to profit financially from a stay in a hospital or by receiving a doctor's services? This question is being raised with greater frequency since research studies indicate that 8 to 15 per cent of those who have prepayment insurance coverage of their hospital, medical, and surgical charges have one or more additional policies.

Because of this duplication of coverage, some commercial health insurance carriers are adding a "No Duplication" clause to many of their group contracts and to some of their direct pay contracts.

. . . If such a clause were included in contracts, it would mean that the Blue plans and any commercial insurance companies involved in covering these subscribers would pay benefits totaling up to the full amount billed for services but would not allow the subscriber, ill as he may be, to make money from prepaid insurance.

If this nonduplication clause were to be included in health care contracts, it would undoubtedly lead to a reduction in the rates charged for such coverage. The rate should fall because (1) duplicate administration would occur less frequently and (2) three or four companies would not pay their maximum on one operation. Look at an example. Blue Shield, Company A and Company B have coverage on you. You have your appendix removed. You collect for Blue Shield, and A, and B. Three groups therefore pay for removal of the same appendix. At the end of the year, the actuaries of all three organizations set up the cost of their policies based on how much usage they had experienced in the past year. Your appendectomy boosts all three firms' figures for the number of operations performed that year. This in turn increases the cost of the policy. What should happen is that the primary insurer (the one who insured the breadwinner) would pay its full fee for the appendectomy and then if there is a remaining unpaid bill, the other two companies divide the cost evenly. The patient gets his bill paid and the companies have fulfilled their obligation. The use of health insurance to pay for unemployment, maid service, or just plain profit will produce overpriced health insurance.

If the Blue plans and the commercial health insurance plans did adopt this nonduplication clause, they would be following a pattern already set in fire insurance and in automobile insurance coverage.

Prepayment of health insurance cost has become an integral part of our American way of life. We have a responsibility to our patients to see that quality health care is provided as reasonably as possible so that our patients would not have to allocate too large a portion of their income on expenditures for this care. These expenditures, of course, include premium payments for health insurance.

We are in an era of rapidly rising health costs, and therefore we must urge our patients to purchase full but not excessive coverage. This would mean, in effect, giving our wholehearted cooperation to all health insurance carriers as they make an effort to eliminate excess payments for health care in order to reduce the cost of their insurance. You and I, as members of the medical profession, know that three problems face us with greater frequency. These problems include (1) a sufficient number of hospital beds; (2) efficient utilization of these beds, and (3) the most efficient expenditure of funds for every phase of health care. It is up to us to see that our patients are able to live within a predictable budget for their health care cost. A nonduplication clause, providing coverage for no more than the full charges, is one way of preserving private medicine in this nation . . .

John T. Stage, M.D.
The Journal of the Florida Medical Association

"Million Dollar" Year

Blue Shield of Minnesota has completed its third successive "million dollar" growth year.

Blue Shield had revenues in 1964 which reached \$14.5 million, or more than \$1 million over the previous year. This is a dramatic gain since 1961 when premiums were about \$10.8 million.

With this financial growth, Blue Shield continued to return approximately 90¢ in benefits from every dollar in premiums collected from subscribers. At the same time, the Minnesota Plan maintained a reserve fund of nearly \$3 and ¾ million, which is the second highest level of reserves since Blue Shield began in 1947.

Blue Shield has already paid out more than \$115 million in benefits for Minnesota physicians since the plan began in 1947.

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Side Effects: Glossitis and allergic reactions, as well as severe anaphylactoid reactions, have been reported as rare side effects. Should significant reaction or idiosyncrasy occur, discontinue medication and institute countermeasures. Use of tetracycline during the last trimester of pregnancy, neonatal period and early childhood may cause discoloration of developing teeth. Reduce usual oral dosage and consider serum level determinations in patients with impaired renal function to prevent possible liver toxicity due to excessive accumulation of antibiotic in the serum.

Precautions: Overgrowth of nonsusceptible organisms may occur. In such cases, discontinue medication and institute appropriate specific therapy as indicated by susceptibility testing. Aluminum hydroxide gel given with antibiotics has been shown to decrease their absorption and is contraindicated. The coloring agents used in Signemycin Syrup and Pediatric Drops may produce red discoloration of stools.

Triacetyloleandomycin, a constituent of Signemycin, administered to adults in daily oral doses of 1.0 Gm. (3 Gm. Signemycin) for periods of more than ten days may produce hepatic dysfunction and jaundice. In the rare patient who requires this high dosage level of Signemycin initially, liver function should be carefully followed and dosage should be reduced, as promptly as possible, to the usual recommended range of 1.0 to 2.0 Gm. per day. Therefore, Signemycin is recommended primarily for the treatment of acute or severe infections, with treatment restricted to a ten-day period. If clinical judgment dictates continuation of therapy beyond ten days, serial monitoring of the liver profile should be carried out, including BSP, transaminase, and cephalin flocculation tests. Changes observed in liver function were reversible following discontinuation of the drug.

Formulas: Capsules: 250 mg. Signemycin (167 mg. tetracycline HCl and 83 mg. oleandomycin as triacetyloleandomycin).

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Syrup: 125 mg. Signemycin (tetracycline equivalent to 83 mg. tetracycline HCl and 42 mg. oleandomycin as triacetyloleandomycin) per 5 cc.

Pediatric Drops: 100 mg. Signemycin (tetracycline equivalent to 67 mg. tetracycline HCl and 33 mg. oleandomycin as triacetyloleandomycin) per cc.

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The high rate of response to Signemycin in these cases is noteworthy because the totals include many patients with difficult-to-treat infections, many whose infections had proved resistant to other agents, and many who had been treatment failures on other therapy.[1-87] In addition the following criteria were used for the cases cited: (1) only published results were used (2) results were confirmed by clinical and/or laboratory findings (3) patients were cured, not "improved" (4) dosage conformed with current recommendations in the United States (5) no other anti-infective agents were used concomitantly (6) no instance of prophylactic use was included in these tabulations.

Condition	No. of Patients	No. Responded To Signemycin
Ear, nose and throat infections	507	465
Respiratory infections	1,028	954
Gastrointestinal infections	425	387
Genitourinary infections	748	684
Skin and soft-tissue infections	1,088	1,036
Bone and joint infections	71	64
Deep-seated or generalized infections	257	251
Obstetrical & gynecological infections	341	320
Miscellaneous conditions	592	570
Totals	5,057	4,731 (93.5%)

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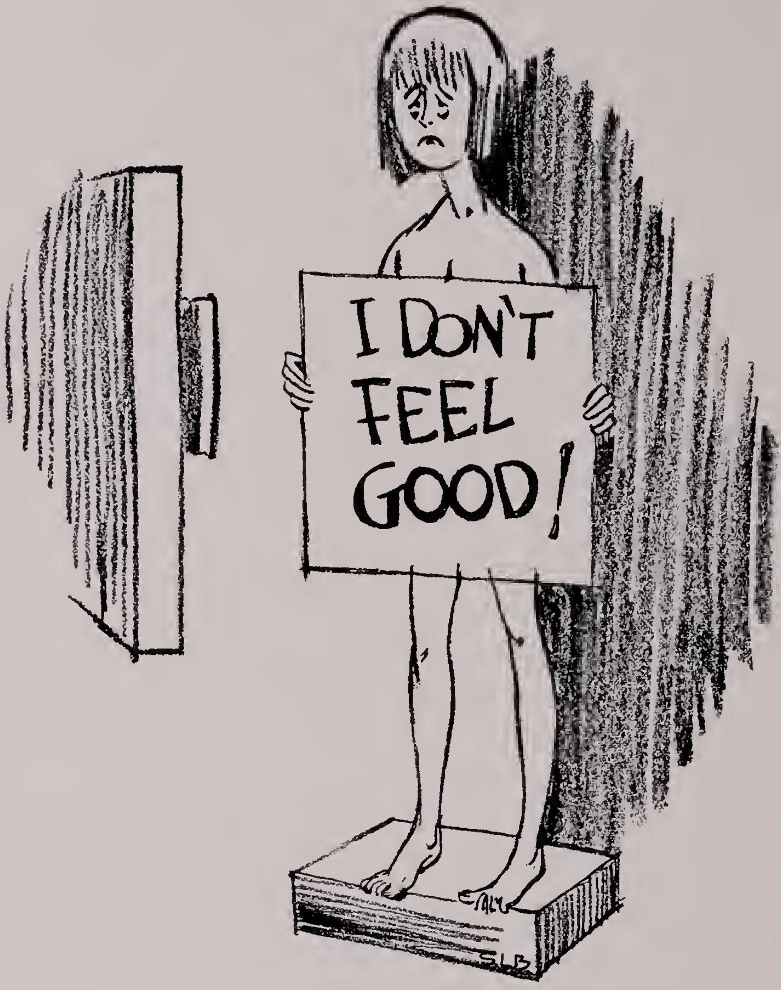

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Continued from Page 260

WANTED: full-time industrial physician for East Central Iowa industrial plant — excellent opportunity. General practitioner preferred, salary open. Immediate opening. Write: MINNESOTA MEDICINE — 299, 496 Lowry Medical Arts Building, St. Paul, 55102.

WANTED AT ONCE — A general practitioner for fine equipped office, 25 bed hospital, Eventide Home and Nursing Home. Call 427-3515 collect or write: Albert W. Steinle, Box 577 Mountain Lake, Minnesota.

USED CLINICAL SUPPLIES FOR SALE. Selling complete clinic — office equipment to X-ray. May be purchased as unit or by item. Contact: C. E. Overby, Madison, Minnesota.

WANTED general practitioner to join clinic close to Minneapolis, anytime between first of the year and the summer. State nationality and religion — Catholic preferred. Write: MINNESOTA MEDICINE — 297, 496 Lowry Medical Arts Building, St. Paul, 55102.

PHYSICIANS WANTED, OREGON COAST —pediatrician, urologist and general practitioner to join group of four internists, surgeon and two GPs. Well established with excellent facilities and reputation. Astoria Clinic, 812 Exchange Street, Astoria, Oregon 325-4111.

PRACTICE FOR SALE. General practitioner. Will practice for six months with prospective buyer to acquaint him with patients. All new equipment from BMR to X ray. See 20-30 patients daily. Reasonable and terms. Dr. A. H. Wolf, 3145 Hennepin Avenue South, Minneapolis, 55408.

EK-2 Burdick excellent condition, rolling stand. Not more than 200 recordings made. Asking $500. Will accept best offer. Owner in residency training. Call 724-7823 or Radiology Department, VA Hospital PA 9-2381.

WANTED general practitioner for St. Paul area. Would like partnership or association basis. Large one doctor office with large well-established practice. Write: Dr. C. M. Kelsey, 1530 West Larpenteur, St. Paul 55113.

MORGAN, MINNESOTA, Wants General Practitioner — Present Physician retiring after 33 years. Opportunity to take over well established practice. Progressive community in the best rural area of Southern Minnesota. Office space and equipment available. Call or write John Hageman, Pharmacist, Morgan, Minnesota. Telephone Morgan No. 96.

PEDIATRICIAN — to head pediatric department of expanding prepaid medical specialty group; Minneapolis-St. Paul; excellent beginning salary; opportunity for teaching and professional pursuits; liberal vacation and benefits. Alfred F. Anderegg, M.D., Medical Director, 2500 Como Avenue, St. Paul 8, Minnesota.

WANTED: General practitioner for Northern Minnesota town. An eight-room clinic located on main street equipped with X ray, etc. Previous practitioner left because of ill health after ten years profitable practice. Golf, hunting and fishing. No initial investment necessary. Write: MINNESOTA MEDICINE — 294, 496 Lowry Medical Arts Building, St. Paul, 55102.

BURNSVILLE MEDICAL CENTER — office space for one, two or group of physicians in Twin Cities fastest growing suburb — ideal for second office. Call Minneapolis 890-1434 or St. Paul 698-8618.

WANTED: General practitioner by established three-man group in own building, fully equipped. Southwestern Minnesota — county seat — population 3,500. New hospital — fine churches — good schools, public and parochial. Golf club — grass greens. Hunting and fishing. Starting salary with opportunity for partnership. No initial investment necessary. Write: MINNESOTA MEDICINE — 199; 496 Lowry Medical Arts Building, St. Paul 55102

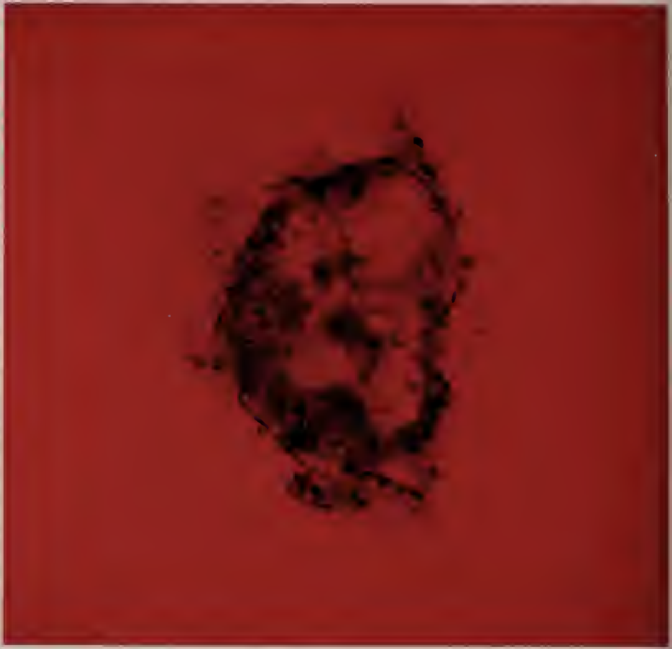
WONDERFUL OPPORTUNITY — Mankato, Minnesota — for a specialist in ENT, OB-GYN and urology in independent practice. Referral practice assured. Office space available. City is 35,000 with trade area of 160,000. Two excellent hospitals with open staff of 60 men, 40 of whom are specialists. Mankato State College enrollment over 8,000 with excellent nursing school. Extremely well-balanced, diversified economy. Write: MINNESOTA MEDICINE — 295, 496 Lowry Medical Arts Building, St. Paul, 55102.

The difference is that a statesman thinks he belongs to the State, and a politician thinks the State belongs to him.

Big men became big by doing what they didn't want to do when they didn't want to do it. — Insurance Salesman

kills Haemophilus influenzae in respiratory infections

Electron micrograph of normal H. influenzae *organism.*



Electron micrograph of H. influenzae *after a 2-hour exposure to a therapeutic (8γ/ml.) dose of PENBRITIN (ampicillin).*

New broad-spectrum penicillin:

- most active antibiotic against *Haemophilus influenzae*[1-3]—a major pathogen in chronic bronchitis and respiratory infections in children
- demonstrated clinical efficacy and safety in chronic bronchitis[4-10]
- more effective than tetracycline in reducing sputum in chronic bronchitis[5]

Usual Adult Dosage: 250 mg. every six hours. *Usual Dosage for Children*—(under 13 years, whose weight will not result in a dosage higher than that recommended for adults) 100 mg./Kg./day in divided doses every six or eight hours for moderately severe infections; 200 mg./Kg./day in divided doses every six hours for severe infections.

Contraindications: (1) Hypersensitivity to penicillin. (2) Infections by penicillinase-producing staphylococci or other penicillinase-producing organisms.

Side Effects: Mild effects, such as skin rashes, diarrhea, nausea and vomiting, have occasionally appeared.

Precautions: As with other antibiotics, precautions should be taken against gastrointestinal superinfection. To date, safety for use in pregnancy has not been established.

Supplied: No. 606—Each capsule contains 250 mg. of ampicillin. Bottles of 16 and 100.

References: 1. Millard, F. J. C., and Batten, J. C.: Brit. M. J. *i*:1159 (April 28) 1962. 2. Ivler, D., *et al.*: Abstracts, Third Interscience Conference on Antimicrobial Agents and Chemotherapy, October 1963, p. 32. 3. Stewart, G. T.: Pharmakotherapia *1*:197, 1963. (Progress in Drug Therapy). 4. Grant, I. W. B., *et al.*: Brit. M. J. *ii*:482 (Aug. 18) 1962. 5. Millard, F. J. C., and Batten, J. C.: Brit. M. J. *i*:644 (March 9) 1963. 6. Oswald, N. C.: Postgrad. Med. *35*:233 (March) 1964. 7. Howells, C. H. L., and Tyler, L. E.: Brit. J. Clin. Pract. *17*:321 (June) 1963. 8. May, J. R., and Delves, D. M.: Thorax *19*:298, 1964. 9. May, J. R., *et al.*: Lancet *ii*:444 (Aug. 29) 1964. 10. Pines, A.: Lancet *ii*:445 (Aug. 29) 1964.

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Meetings and Announcements

Be very circumspect in the choice of thy company. In the society of thine equals thou shalt enjoy more pleasure; in the society of thy superiors thou shalt find more profit. — Quarles

FEBRUARY

Minnesota Academy of Medicine, Regular meeting — February 10, 7:00 p.m., Town and Country Club, St. Paul.

St. Louis County Medical Society, Executive Comm. — February 11, 6:00 p.m., St. Luke's Hospital, Duluth, Regular meeting at 8:00 p.m.

Ramsey County Medical Society, Business & Program — February 22, 8:00 p.m., 15th Floor Lowry Medical Arts Building, St. Paul.

American College of Chest Physicians Postgraduate Course on Recent Advances in the Diagnosis and Treatment of Diseases of the Heart and Lungs, February 1-5, Fontainebleau Hotel, Miami Beach, Florida. Contact: College of Chest Physicians, 112 East Chestnut Street, Chicago.

70th Sioux Valley Medical Association Meeting, February 18 and 19, Sioux City, Iowa, at the St. Vincent Hospital and Sheraton Warrior Hotel. Contact: H. E. Rudesdorf, M.D.; 2417 Pierce Street, Sioux City, Iowa.

American College of Surgeons Sectional Meeting in Philadelphia, February 15-17, Bellevue-Stratford Hotel. Contact: Mr. T. E. McGinnis, American College of Surgeons, 55 East Erie, Chicago.

MARCH

Hennepin County Psychiatric Society, March 1, 6:30 p.m., Leamington Hotel, Minneapolis.

Zumbro Valley Medical Society, Regular meeting — March 3, 8:00 p.m., Plummer Hall, Rochester.

Minnesota Academy of Medicine, Regular meeting — March 10, 7:00 p.m., Town & Country Club, St. Paul.

St. Louis County Medical Society, Executive Comm. — March 11, 6:00 p.m., Regular meeting — 8:00 p.m., St. Mary's Hospital, Duluth.

Ramsey County Medical Society, Business & Program — March 29, 8:00 p.m., 15th Floor Lowry Medical Arts Bldg., St. Paul.

Mayo Clinic and Faculty of Mayo Foundation Clinical Reviews, March 15, 16 and 17 and March 22, 23 and 24. Mayo Civic Auditorium in Rochester. Contact: M. G. Brataas, Secretary, Mayo Clinic in Rochester.

Twenty-eighth Annual Meeting of the New Orleans Graduate Medical Assembly, March 8, 9, 10 and 11, Roosevelt Hotel in New Orleans, La. Details may be obtained at the Office of Assembly, 1430 Tulane Avenue, New Orleans, La. 70112.

American College of Surgeons and graduate nurses, in Seattle, March 8-11, Olympic Hotel and Palomar Theatre. Contact: College at 55 E. Erie Street, Chicago.

American College of Physicians golden anniversary session, March 22-26, Conrad Hilton Hotel in Chicago. Contact College at 4200 Pine Street, Philadelphia, Pa.

University of Colorado postgraduate course in medical technology, March 15-20, in Denver. Contact University, 4200 East 9th Avenue in Denver.

ANNOUNCEMENTS

Part II examination will be conducted by the American Board of OB-GYN at Edgewater Beach Hotel in Chicago, April 26-May 1. Applications will be accepted in the office of the secretary during April and May. Contact: Clyde Randall, 100 Meadow Road, Buffalo, N. Y.

* * *

The 28th annual meeting of the New Orleans Graduate Medical Assembly will be held March 8-11, at the Roosevelt Hotel. Details of the New Orleans meeting are available at the office of the Assembly, 1430 Tulane Avenue, New Orleans, La. 70112.

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the long-acting diuretic

Indications
Many types of edema involving retention of salt and water.
Contraindications
Hypersensitivity, and most cases of severe renal or hepatic disease.
Precautions
Reduce dosage of concomitant antihypertensive agents by at least one-half. Discontinue if the BUN rises or liver dysfunction is aggravated. Electrolyte imbalance and potassium depletion may occur; take special care in cirrhosis or severe ischemic heart disease, and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended.
Side Effects
Constipation, dizziness, dysuria, headache, hyperglycemia, hyperuricemia, leukopenia, muscle cramps, nausea, purpura, thrombocytopenia, transient myopia, urticaria, vomiting and weakness.
Average Dosage
One tablet (100 mg.) daily with breakfast.
Availability
Tablets of 100 mg. in bottles of 100 and 1000.
For full details, see the complete prescribing information.

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Not very high. In terms of one week's therapy, that is. The usual dosage is just one tablet per day. Very often, the dosage is even lower. So a week's therapy doesn't amount to much.

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Each tablet contains:

Salicylamide	250 mg.
Acetaminophen	250 mg.
Ascorbic acid (Vitamin C)	25 mg.

a working analgesic for the active arthritic

—rapidly relieves early morning stiffness and arthritic pain. It promises a quicker response in most patients because its analgesic ingredients need no metabolic conversion before they act. As a combination of two prominent analgesic drugs, Arthralgen can often establish smoother, more complete pain relief because it synergistically produces more efficient analgesia on lower dosage levels of each.

two proven pain relievers

Arthralgen combines two better-tolerated, time-tested analgesics, acetaminophen and salicylamide, into a pharmacologically sound and therapeutically effective formulation. As Arthralgen, it penetrates tissues promptly and relieves pain rapidly with less likelihood of gastric irritation than aspirin.

sodium-free

Arthralgen contains no sodium. Therefore, it is often a safer and more suitable analgesic for use in the long-term treatments of arthritic patients who have other conditions which require sodium restriction.[1]

ARTHRALGEN®-PR (Arthralgen with prednisone)

Each tablet contains:

Salicylamide	250 mg.
Acetaminophen	250 mg.
Ascorbic acid (Vitamin C)	25 mg.
Prednisone	1 mg.

To help provide dosage flexibility in patients who require steroids, the basic Arthralgen formula is also available combined with prednisone as Arthralgen-PR. Prednisone is favored as the more advantageous steroid for use in Arthralgen-PR because it shows less tendency toward sodium retention, potassium excretion, and steroid-induced hypertension than that which often accompanies the use of cortisone and ACTH.[2]

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Arthralgen and Arthralgen-PR are indicated in the management of rheumatoid arthritis, acute gouty arthritis, rheumatoid spondylitis, osteoarthritis, bursitis, fibrositis, and neuritis. Arthralgen may be used for analgesia in colds, flu, and various myalgias.

DOSAGE: One or two tablets four times a day. After remission of symptoms dosage should be reduced to the minimum maintenance level.

SIDE EFFECTS: Nausea, GI upset, or mild salicylism may rarely occur. Symptoms of hypercorticoidism dictate reduction of dosage of Arthralgen-PR.

PRECAUTION: Reduction in dosage of Arthralgen-PR given over a long period should be gradual, never abrupt.

CONTRAINDICATIONS: Hypersensitivity to any ingredient.

As with any drug containing prednisone, Arthralgen-PR is contraindicated, or should be administered only with care, to patients with peptic ulcer, tuberculosis, nephritis, diabetes mellitus, acute psychoses, Cushing's syndrome (or Cushing's disease), overwhelming spreading (systemic) infection, or predisposition to thrombophlebitis.

Arthralgen-PR is generally contraindicated in patients with uremia and viral infections, including poliomyelitis, vaccinia, ocular herpes simplex, and fungus infections of the eye. It is also contraindicated in patients with chicken pox or susceptible persons exposed to it.

SUPPLY: Arthralgen (white, scored) and Arthralgen-PR (yellow, scored) tablets are available in bottles of 100 and 500.

REF: 1. Boreus & Sandberg, ACTA. PHYSIOL. SCAND., 28:266, 1953. 2. Cohen, et al.: J.A.M.A., 165:225, 1957.

Physician's Diary

Be cautious with whom you associate, and never give your company or your confidence to those of whose good principles you are not sure. — Coleridge

Dr. Carl L. Lundell of Granite Falls was one of the featured speakers at the first National Conference on Areawide Health Facilities Planning held at Bal Harbour, Florida, in November. **Dr. Lundell** spoke on the subject "Planning for a Rural Community."

* * *

At the New Prague Rotary club in December, **Dr. B. H. Pearson** and **Dr. F. H. Buck**, both of Shakopee, recently described their experiences gained from a visit to Northern Rhodesia, Africa, last summer, and of the building of a leprosarium. The Shakopee Rotary club has joined the Shakopee doctors in furthering this project and have invited other civic organizations to participate.

* * *

Dr. S. Francis Ceplecha of Redwood Falls spoke at the annual meeting of the Wright County School Officer's Association held in Buffalo in December. **Dr. Ceplecha** spoke on "The Precise Principles of Education."

* * *

NEW LOCATIONS: **Dr. W. E. Johnson** will leave Morgan to become a staff doctor at the St. Cloud Veterans hospital . . . **Dr. Lawrence Poston** will practice in Caledonia . . . **Dr. A. D. Davidson** of Caledonia has begun a fellowship with the Mayo Foundation at Rochester in ophthalmology . . . **Dr. Laddie E. Stover** and **Dr. Wayne L. Campbell** have formed a partnership and begun the practice of medicine in Waseca . . . **Dr. R. D. Schrantz**, Itasca Clinic, will leave his practice in Park Rapids to take a four year course in pathology in Phoenix, Arizona . . . **Dr. Donald M. Brink** has closed his office in Hutchinson and will assume his appointment at the state hospital at St. Peter . . . **Dr. William Kozel** of Morris has established office hours at the clinic wing of the Hoffman Nursing Home in Hoffman . . . **Dr. B. H. Johnston** of Litchfield has opened up a medical practice in the Ivanhoe Clinic Building in Ivanhoe.

Dr. C. D. Creevy, professor and chief of Urology, University of Minnesota Hospitals, is taking a quarter leave between January 15th and April 15th from his duties at the hospital.

* * *

Dr. Rodney W. England of St. Paul has been certified as a Diplomate of the American Board of Internal Medicine.

* * *

Dr. J. W. Griffin was elected chief of staff at the annual meeting of the Bemidji hospital staff. **Dr. H. C. Reed** was named vice president and **Dr. L. A. Olson**, secretary-treasurer.

* * *

Dr. Paul Dunstan of Willmar is listed in the newest editions of "Who's Who in Minnesota" and "Who's Who in the Midwest." **Dr. Dunstan** is medical director of the West Central Mental Health Clinic and chief of staff of the Wilmar State Hospital.

* * *

Dr. Harry Burich was elected president of the medical staff of the Olmsted Community Hospital at Rochester. **Dr. Conrad W. Baars** was elected vice president and **Dr. Werner Kaese** was elected secretary-treasurer.

* * *

Dr. Glenn Brown of Halstad was elected president of the Red River Valley Medical Society, and **Dr. Vincent Hunt** of Red Lake Falls was named vice president. **Dr. R. O. Sather** of Crookston was reelected secretary-treasurer.

* * *

Dr. Michael A. Howard, son of **Dr. M. I. Howard** of Mankato, was awarded second prize for his scientific presentation made at the Junior Fellow Division meeting of the American College of Obstetricians and Gynecologists in Winnipeg recently. **Dr. Howard** is presently completing a residency at Cook County Hospital.

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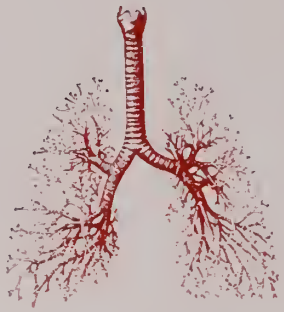

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President's Letter

In view of the widespread discussion about methods of medical care for the American people, it seems pertinent to review the policies of the American Medical Association on this subject. The American Medical Association has always taken the position that no one should lack medical care because of inability to pay for it, and traditionally physicians have supported this principle and have annually provided free care which is estimated to amount to several hundred million dollars. The American Medical Association has repeatedly opposed public care for those who are able to pay their medical bills and for whom no governmental responsibility is evident. Such responsibility has been recognized by organized medicine, but always for a specific need.

From an early date the American Medical Association has supported a Public Health Service. The Armed Servicemen, together with their dependents, retired personnel and those disabled in service have been cared for at government expense with the cooperation of the American Medical Association. Most of this care is rendered by physicians who are employed by the government or are in the Armed Services, but some of it is provided by contract with private physicians.

The American Medical Association has steadfastly insisted on freedom for the patient to choose the physician or the method of health care of his choice, and it has been concerned that in any plan the physician have freedom to provide the best possible care.

When a financial need exists, the American Medical Association has asked that the responsibility be discharged at a level as close to the patient as is possible, and it has opposed direct use of federal funds on the assumption that at a national level of administration the physician's control to ensure the best medical care may be lessened. The association has endorsed the principle that when federal aid is necessary, it should supplement state or local funds and be administered through state or local governmental agencies.

The American Medical Association supports the principles of voluntary health insurance and the prepaid Blue Cross and Blue Shield plans, including coverage for catastrophic illness through major medical insurance. Direct federal subsidization of prepayment plans and health-insurance companies has been considered undesirable. This does not, of course, include the purchase of such care for federal employees by the government as an employer. A number of states have purchased insurance and service plans for the medically indigent with the full approval of the organized medical societies and the American Medical Association.

In December, 1964, at Miami the House of Delegates clarified the American Medical Association's position by adopting the following resolution: "The House of Delegates urges the component associations of the American Medical Association to stimulate the state and local governments to seek the fullest implementation of existing mechanisms including the voluntary health insurance principles to the end that everyone in need, regardless of age, is assured that necessary health care will be available."

With the foregoing principles outlined as a background, it will be apparent why the

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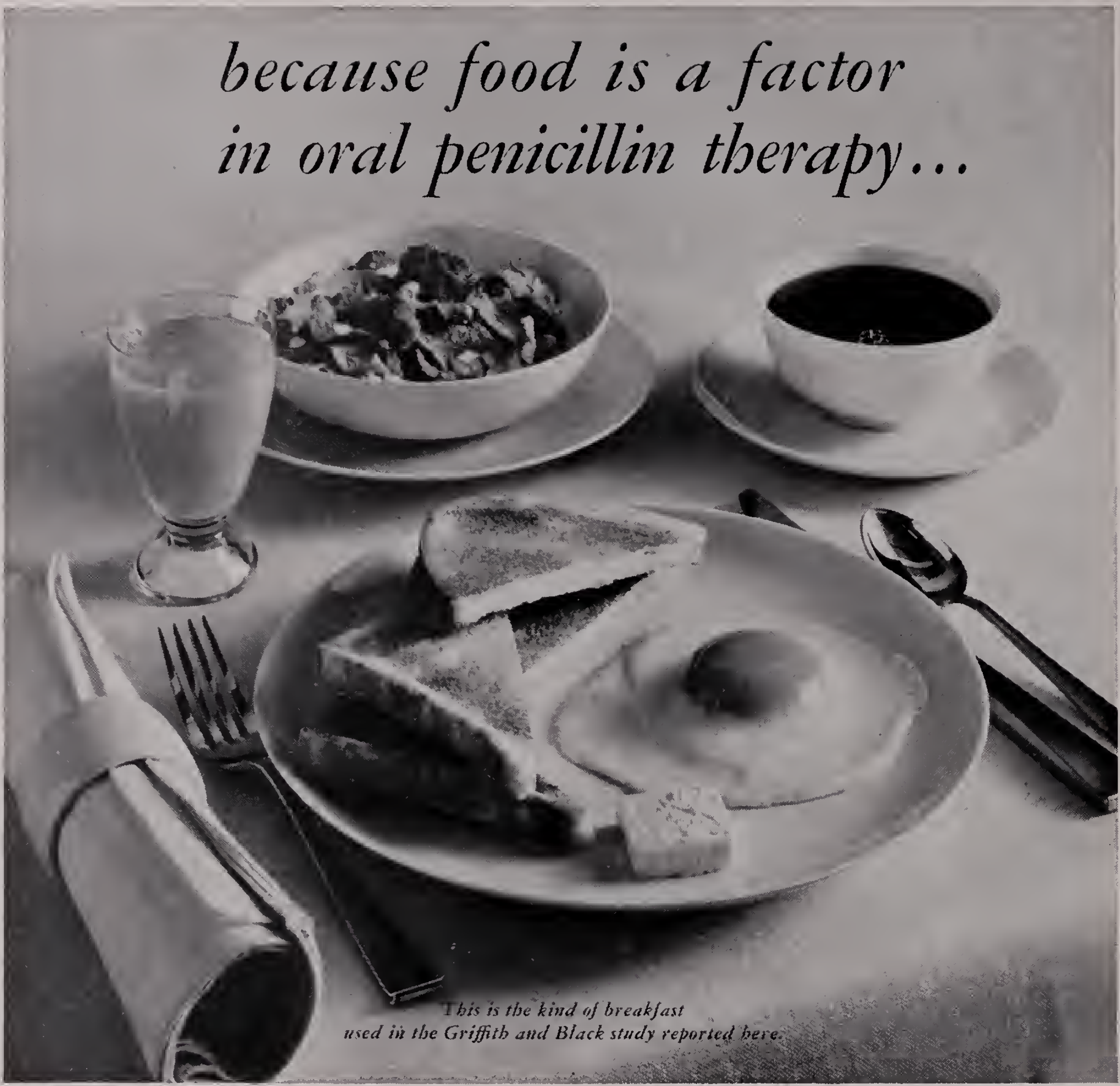

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Premalignant Lesions of the Colon and Rectum[*]

A perplexing problem influencing the practice of all clinical physicians.

ROBERT TURELL, M.D.**
ALBERT S. LYONS, M.D.**
New York, New York

A CONTROVERSY is in progress regarding the "premalignant" status of a number of polypoid and inflammatory lesions of the anorectocolonic tube. These include (1) adenomas; (2) chronic ulcerative colitis; (3) venereal diseases such as venereal lymphogranuloma, and Donovanosis,*** and (4) fistulous and sinous tracts. Not only is there dissension in interpretation of the basic facts; there is not even agreement on the precise definition of the words "premalignant and precancerous." To some clinicians these terms mean the inevitable transformation from a benign to a malignant process. To others, they suggest only a greater chance of developing cancer. Agreement on terms of polyp and the various types of adenomas is most essential, and the reader is referred to our most recent paper on this subject.[1]

In presenting opposing views we have been guided by Charcot's long remembered saying, "Disease is very old and nothing about it has changed. It is we who change as we learn to recognize what was formerly imperceptible." What is "irrefutable evidence" today may later be proved erroneous. The great issue here is not agreement but debate which may ultimately lead to a better understanding of the problem.

Adenoma

If all adenomas do eventually become invasive cancer, then all adenomas should be removed before they become cancer. If some but not all adenomas do become cancer, then there should be ways of distinguishing which are "premalignant" and which are benign. The morbidity and mortality of the various methods of surgical removal of adenomas as compared with the chances of transformation to cancer must be given consideration.

---

*Presented at the Minnesota State Medical Association Annual Meeting in Rochester, May 19, 1964.

**Surgical Services of Mount Sinai Hospital and Albert Einstein College of Medicine.

***See Test Your Word Score Page 359.

Many pathologists and clinicians believe that most colonic adenomas eventually become cancer. The evidence consists of: (1) the allegedly similar distribution of cancer and adenomas; (2) the younger age incidence of adenoma and the older age occurrence of cancer; (3) the high incidence of adenomas in patients with cancer of the colon; (4) the frequency of colonic cancer among patients with colonic familial polyposis, and (5) the demonstration in individual specimens of a transition from adenoma to adenocarcinoma.

Similar Distribution

Authors who favor the direct relationship concept claim that adenomas and cancer occur with similar frequency in the same segments of the bowel. However, even the actual incidence of adenomas is not clearly established. Reported frequency has varied from 1.7[2] per cent to 69 per cent.[3] Wide differences exist in the interpretation of mucosal excrescences and in the methods of evaluating different populations.[4] With such conflicting data, considerable confusion is bound to result from trying to correlate incidence and distribution.

In 1939, Klemperer[5] reviewed the literature on adenomas and reported that the autopsy findings of Reichel and Staemmler in 1924 were *not* supported by more recent reports. He noted that whereas only 44 per cent of adenomas occurred in the rectum and sigmoid, 75 per cent of colonic cancers occurred in these same locations; further he noted that in patients beyond 40, adenomas are too frequent to allow statistical age comparisons with the incidence of cancer. He therefore concluded that there was no evidence for a direct relationship between adenomas and cancer. On the other hand, Swinton and Haug[6] came to the contrary conclusion on the basis of 1,843 autopsies, in which 73.5 per cent of cancers and 52.2 per cent of adenomas were found in the distal colon. Thus, with data similar to Klemperer's their interpretation was diametrically opposite.

Bockus et al.[7] and Koppel et al.[8] reported that among two groups of people, one with and the other without adenomas, both developed the same numbers of cancers. Spratt et al.[9] used statistical analyses and discovered that both adenomas and cancer occurred with greatest frequency in the cecum; but in the rectum and sigmoid, cancers were considerably more frequent than adenomas. This would mean that even if all adenomas were to become malignant, this transformation could *not* account for all the cancers found. Some cancers would have had to arise *de novo,** without first being adenomas.[10]

Age Succession

Buie and Brust[11] stated that there is a nine-year difference in the average age of patients with adenomas and cancer, and their inference was that these years represented the time needed for the adenomas to become cancer. However, Andren[12] has reported a higher incidence of adenomas in the first decade than in either the second or third, and Bockus et al.[7] and Enterline[13] noted that the average age of patients with adenomas resembled the average age of patients with cancer.

Spratt et al.[9] indicated that after the age of 50 cancers were found in polyp-containing and polyp-empty colons with the same relative frequency, but in younger patients (30 to 49 years old) there was a definite increase of cancers among those with adenomas.

Incidence of Adenomas in Patients With Cancer

Dukes,[14] and Goligher[15] found that a high proportion of colons with cancer also had adenomas. A study by Rider et al.[16] presented strong evidence that patients with multiple adenomas are twice as likely to develop cancer as those with solitary adenomas. However, these authors concluded that their findings did *not* corroborate a direct relationship between adenoma and cancer, but instead indicated that the mucosa of people with adenomas has an increased tendency to form more neoplasms, cancers as well as adenomas.[17]

Cole et al.[18] studied the records of 87 patients with invasive cancer of the colon who survived operation and found that those with adenomas had a lower incidence of involved lymph nodes and a higher survival rate than those without associated adenomas. Recalling that Valdes-Dapena and Beckfield[19] had previously described the earliest change in the formation of an adenoma to be thickening of the submucosa, Cole and his co-workers suggested that this thickening might act as a barrier to the development and spread of a cancer. Contrarily, the study by Grosberg and Galambos[20] did not reflect an enhanced resistance to neoplasia, but rather an increased "susceptibility" to cancer in colons with adenomas.

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*See Test Your Word Score Page 359.

Incidence of Cancer in Patients With Multiple Polyposis

Congenital Familial Polyposis

Dukes[20,21] reported that among 700 members of 57 families, 251 developed multiple polyposis. Invasive cancer developed in 114 of the first 156 studied.

However, what would seem to be an obvious close relationship to malignancy is not so clear-cut on more detailed study. For example, numerous authors have emphasized that the patients with familial polyposis may have an altered hereditary response of their colonic mucosa and therefore the polyps themselves may not be the origin of the cancers. Spratt et al.[9] showed that the distribution of colonic cancers in patients with familial polyposis was exactly the same as in colons without any adenomas. These observations do *not* deny the occurrence of cancer in people with congenital polyposis but instead indicate that the occurrence of cancer does *not* follow the distribution of the adenomas!

Assuming two types, one familial and the other nonfamilial, the comparisons made between solitary and familial cases have not revealed differences in size, number, or distribution of the polyps and tumors, or any differences in the age of onset, symptoms, or course of the disease. Individual patients with multiple polyposis appear to develop carcinoma after the same average period (about 15 years). Also, the average age of death is the same for both solitary and familial forms. It may be that some of the solitary cases are merely the first manifestation of a gene mutation, so that although these patients have not inherited polyposis from their forbears, they may transmit the disease to their offspring. Thus, the solitary and the familial types may be regarded as examples of the same disease.

Congenital polyposis may be associated with other abnormal growths in the body, such as fibromas, lipomas, fibrolipomas, epidermoid cysts, leiomyomas, dermoids, desmoids, osteomas, bony exostoses, and fibrosarcomas. The finding of these lesions should suggest the possible presence also of familial polyposis.

The Peutz-Jeghers Syndrome

In this syndrome, the polyps are predominantly located in the jejunum but may occur anywhere in the entire gastrointestinal tract. Usually, but not always,[23,24] mucocutaneous melanin pigmentation on the lips and gums is associated. On occasion, the pigmentation involves the palms and soles and their appendages. This syndrome is believed to be familial and hereditary, as a simple Mendelian dominant (gene), although isolated (sporadic) cases have also been reported

Until a few years ago, there existed considerable confusion in interpretation of pathologic data. The disease is now considered a specific pathologic entity with definite histologic features that are distinguishable from the pathologic patterns of other polypoid lesions of the alimentary tract.[25-28] Most workers[25,27] insist that the intestinal lesions are hamartomas.* Burdick et al.[24] have questioned the hamartomatous nature of this lesion; they feel that the presence of more than one major cell type cannot be considered proof of their hamartomatous nature.

Except for a rare dissent,[28] there is virtually unanimous agreement in the recent literature on the total absence of any cancer potential in the Peutz-Jeghers polyps.

The melanin pigmentation is considered one of the main symptoms of this syndrome. However, Turell et al.[23] have reported three cases of circumoral pigmentation without clinically detectable polyposis anywhere in the alimentary tract, and two that were associated with true adenomas in the rectosigmoid. Burdick et al. had also observed pigmentation without polyps in their extended study of one large family. It should also be remembered that melanin pigmentation may be physiologic in some persons, may occur in the familial form of polyostotic fibrous dysplasia (Albright's disease), or may follow the administration of certain drugs such as quinacrine hydrochloride.[29]

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*See Test Your Word Score Page 359.

Juvenile Polyp (Also known as congenital cystic polyp; retention polyp, and juvenile adenoma)

Gelb et al.[30] reported 19 polyps in children (two to 17 years of age). Three were typical adenomas; eight were juvenile polyps (with granulation tissue replacing mucosa and stroma, and with neutrophilic and eosinophilic infiltration); five were purely inflammatory, and three showed features of both adenoma and juvenile polyp. The juvenile polyps were considered adenomatous polyps with the inflammatory changes that follow surface erosion.

Roth and Helwig[31] have suggested that the juvenile polyp may actually be formed as a result of the cycle of ulceration and inflammation of the intestinal mucous membrane.

Whatever the pathogenesis of juvenile polyps may be, their insignificance as precursors of malignancy can be judged by the fact that not a single proved case of cancer has been found to arise in a juvenile polyp in a combined series of over 500 cases gleaned from the literature. Ackerman[32] has also stated that this type of polyp may not be a true neoplasm.

Histologic Evidence for Malignant Transformation

Interpretation of the available data is not simple. Not all pathologists agree on the precise criteria of malignancy in adenomas,[33,34] and the evidence for malignant change in adenomas is inconclusive.

Fractional Biopsies

The ultimate discovery of carcinoma after repeated benign fractional biopsies only emphasizes the limitations of fractional biopsy, rather than any transformation by the polyp. Furthermore, Colvert and Brown[35] have shown that in patients who refused to have their adenomas removed, the later incidence of cancer was essentially the same as in another group who did have their polyps removed. Thus the adenomas were benign or malignant at their origin and did not change into cancers.[36]

Transition from Benign to Malignant

Concerning the histologic finding of transition from adenoma to carcinoma in the same specimen, as originally championed by the German pathologists, the method of classification of the stages of atypism has been and often still is highly arbitrary.[37] Kaufmann[37] and Tonnesen[37] were among the first to criticize the interpretations. Yet Helwig[38] and others have continued to claim that there is a gradual transition from benign adenoma, through the stages of localized anaplasia, to clear (though low-grade) malignancy. Buie and Brust[11] have stated that they have found no evidence of higher grade of malignancy developing from an adenoma. Lane and Lev[39] have concluded, however, that most colonic cancers arise from adenomatous epithelium.

Most contemporary pathologists do not describe transitions through the stages of atypism to carcinoma. Some have described areas of frank invasive cancer in otherwise benign-appearing adenomas. Swinton and Warren[40] and others[38,41,42] reproduced photomicrographs of lesions considered to represent the transitions. Enterline[13] found a few remnants of what he interpreted to be the original adenoma, but he also conceded that others might consider the remnants to be highly differentiated adenocarcinoma and not adenoma.

Contrarily, after reviewing representative sections from 298 polypoid cancers, Ackerman[9] found no vestiges of a benign predecessor and agreed[33] with Castleman[43,44] that adenomas have a negligent malignant potential. He further argued that the current rate of small, infiltrating cancers arising from nonadenomatous mucosa can be shown statistically to be sufficient to account for all cancers of the colon.

There is considerable confusion on what is invasive cancer (in spite of agreement among most recent authors that local removal is entirely adequate for noninvasive cancer). Different interpretations of identical data can lead to completely different conclusions, as demonstrated by Castleman and Krickstein.[43] (The newer sophisticated studies reported elsewhere[1] may be of real help in this regard.)

It is of interest to note that Earle, as early as 1911, had written, "Non-malignant tumors are in fact less liable to originate malignant disease than are the normal morphological elements of the body itself."[45] Pennington in 1923 also believed that there was no evidence that a benign adenoma later becomes malignant.[45]

Recommended Procedure

No matter what the malignant potential of adenomas may be, we believe that all symptomatic adenomas should be extirpated. Removal is necessary in order to obtain a total biopsy, the only means of determining unequivocally the presence or absence of invasive cancer. There are few valid exceptions to this requirement. Particularly the short pedicled or sessile lesions should be removed, because they can be mimicked by cancer.

Poor Risk Patients

On the other hand, the asymptomatic small adenoma with a long pedicle, discovered on X-ray studies, in a poor risk patient may *not* require extirpation. However, even here it must be realized that malignancy may be present in the stalk.[36] In spite of the current belief[44,46] that metastases from cancers on a pedicle are negligible, the only way to determine the character of an adenoma is to remove it for histologic examination. Nevertheless, the pedunculate, smooth-contoured lesion beyond the reach of the sigmoidoscope in a patient who is a subnormal risk is sometimes better left alone.

Location of the Adenoma

Various aids are available at laparotomy to find adenomas: palpation of the gut, transillumination coloscopy through small incisions with and without insufflation, and extended colotomy incisions.[47] Actual palpation of the exposed polypoid lesion for the presence of induration is a surprisingly reliable indication of invasive malignancy. Frozen section examination of colon polyps unfortunately is often not helpful.

Removal of the Polyp

Polypectomy through colotomy incisions apparently is adequate for adenomas with long, true pedicles. Welch[48] and Castleman[43] have suggested that traction by the surgeon may give a false impression of the presence of a pedicle. However, follow-up study by us and by others indicates that a conservative operation is sufficient for the treatment of the mucosal lesion that is liftable (and therefore not fixed) from the underlying submucosal structures.

Contrarily, when any segment of the stalk, regardless of its length, is invaded by cancer, a segmental intestinal resection at the very least is needed, in our judgment. Conflicting opinions have been reported by McLanahan et al.,[49] Turnbull,[50] Dukes and Lockhard-Mummery.[22]

Subtotal colectomy and ileoproctostomy is still the most favored operation for the treatment of diffusely distributed multiple sessile or short-pedicled adenomas, as well as for congenital familial polyposis. Regression and spontaneous disappearance of the remaining rectal adenomas have been reported in isolated instances.[51,52]

Villous Adenoma

Villous adenoma has been assumed to originate in cells of the surface mucous membrane,[36] whereas adenoma is said to arise from the cells lining the intestinal mucous glands;[21] but Cole has suggested that both types may begin in the surface cells.[52a]

Combinations of villous and smooth adenomas in the same lesion and separately in the same colon have been seen frequently. We have encountered villous adenomas on pedicles and even on long stalks. Neither cell atypism nor mitoses are indicative of clinical malignancy. Furthermore, the size of the adenoma bears no relationship to the occurrence of cancer. We have observed invasive cancer in lesions smaller than 1 cm. in diameter and extremely large lesions without cancer.[36]

Precursor of Cancer

General opinion favors the belief that villous adenomas are often precursors of cancer.[46,53] Yet, except for the higher incidence of unequivocal cancer observed at the time of the initial examination, as compared with smooth adenomas, clear-cut evidence is not available that villous adenomas are more apt to undergo malignant degeneration.[21]

It is not determinable whether villous adenoma with invasive cancer was originally noncancerous. The often seen large villous adenoma of long duration which remains benign lends support to the concept that the coexistence of invasive cancer with villous adenoma may be guilt by association and not necessarily guilt by transformation. While the discovery of invasive cancer in a villous adenoma might be in keeping with the belief that villous adenomas may be subject to malignant change, a painstaking search of the literature has so far disclosed only one author[54] who himself has vaguely (certainly contestably) observed a benign villous adenoma undergo malignant transformation (actual invasive cancer) during his period of observation. In this instance, the report stated that a villous adenoma had been removed "which was reported by the pathologist to be a benign tumor. Four months later there was a recurrence which proved to be invasive carcinoma." The author added, however, that he was "willing to admit that the original diagnosis may have been in error."

Identification of Malignancy

The key to the dilemma, as in the problem with smooth adenomas, is in the criteria for malignancy. Interestingly, until about a decade ago, pathologists seldom reported noninvasive malignancy in villous adenomas. Recently more and more descriptions differentiate between noninvasive and invasive cancer.

The simultaneous occurrence of benign villous adenomas in one area of the colon and invasive cancer at another site in the colon is not uncommon. The character of the two lesions can often be distinguished roentgenologically. The radiologic features of villous adenoma have been well described by Wolf.[55] Clinically, with the adenoma accessible to palpation, induration is a strong indication that invasive cancer is present in the adenoma.

General opinion also subscribes to the belief that recurrence following local removal is a characteristic of villous adenoma. In our experience, and from the observations of others,[56,57] the rate of recurrence of smooth and villous adenomas is virtually the same. Furthermore, the recurrences have continued to be benign, following the removal of a totally benign villous adenoma.

On the other hand, it is also true that an invasive cancer may lurk in the depths of a villous adenoma, to be discovered only when the adenoma has been removed or after repeated extirpations.

How is the villous adenoma best treated? The methods advocated depend on the attitudes toward the cancer potential, and range from the radical to the conservative forms of surgical procedures.

Treatment

The conservative methods include local excision,[53,58] the Rehn-Delorme operation,[59] and electrocoagulation. The opposition to electrocoagulation is based on the concept that constriction of the rectum[54] may result and that multiple applications of electric energy to a tumor may lead to a "violently active malignant growth surge."[60] We have not been able to confirm this belief, after the use of electrothermic, amputative procedures, with either the snare or double loops resector. The "growth surge" is not due to the electrothermia but rather to an infiltrating cancer that was unrecognized at the initial treatment.

Resection of the segment of bowel containing a villous adenoma is considered good treatment. Whenever possible any site in the colon and rectum above the lower few inches can be radically excised as for cancer. Technically, even a large benign rectal villous adenoma can be totally extirpated with retention of the rectum.[61,62] However, an abdominoperineal resection of the rectum for a benign villous adenoma, as recommended by some,[63-65] is too high a price to pay. An unnecessary extensive resection when intestinal continuity can be restored is permissible, but the imposition of a permanent colostomy for a benign lesion is not warranted. The more radical operation can be performed if the histologic examination of the specimen removed by conservative procedures reveals invasive cancer. Some time may be lost, but many anal sphincters may thus be saved. Liechty and Raterman,[57] Dreese,[56] and Hightower[65a] hold similar views.

In addition, we have treated villous adenomas with noninvasive focal cancer by conservative procedures without recurrence when the surgical risk was high or when loss of the rectum would have been otherwise necessary. Hightower[65a] has also treated "villous adenoma with malignant foci" (the equivalent of noninvasive cancer) by a conservative method.

Of course, when invasive cancer coexists with villous adenoma, radical surgical operations, adhering to cancer principles, are mandatory.

In sum, meager evidence exists for the transformation of the smooth, lobulated, benign adenoma into invasive, metastasizing cancer.

On the other hand, the opinions of most authorities subscribe to a definite cancer potential of the villous adenoma. On the basis of our own observations, we consider the villous adenoma dangerous because it may contain an invasive cancer, but not because it is necessarily of itself a precursor of malignancy.

Fractional biopsy should be abandoned in favor of total biopsy, whenever possible. Resection for histologic verification of all symptomatic polypoid lesions (villous or smooth) is advisable, regardless of anatomic location.

Ulcerative Colitis

The first instance of cancer found in ulcerative colitis was reported by Yeomans.[66] Since then many papers[67-70] on the subject have appeared.

Incidence of Malignancy

In general, it is fair to state that the overwhelming consensus considers ulcerative colitis a dangerous precursor to cancer.[71-77] The incidence in ulcerative colitis has been variously estimated from 0 to 33 per cent.[78-80] Reports of cancer in children with colitis have also appeared.[81,82] Malignancies in ulcerative colitis arise at an earlier age — in the fourth versus the sixth decade. Cancer has occurred in even very small rectal stumps.[83] The time interval between the known onset of the inflammatory process and cancer has been variously estimated as from five to 12 years.[84,85] Aylett, a strong advocate of ileorectal anastomosis to diseased bowel, has nevertheless been reluctant to perform this procedure in long-standing ulcerative colitis, as rectal cancers have occurred in his patients often enough to be striking.[86]

On the other hand, a small but authoritative body of opinion[87-89] still holds that the association of ulcerative colitis and cancer is coincidental. They believe that in many cases the cause of the cancer is an undetected familial polyposis. The polypoid lesions are either hidden or destroyed by the superimposed inflammation. The reported statistics are regarded as deceiving because they are selected, not random, and stem from either surgical specimens or necropsies, making them highly selective and weighted heavily with severe disease. They also call attention to the not too well known fact that infrequently ulcerative colitis occurs after the onset of the cancer. The role of adenomas is no clearer in ulcerative colitis than in normal colons.

Whatever the ultimate truth may be, the important consideration today is whether the risk of cancer is great enough to require removal of the colon and rectum in any patient with long-standing ulcerative colitis (over 10 years),[70,85] regardless of symptomatology. On the basis of present knowledge, we would say, "No!"

In the first place, the highest incidence of malignancy is in the bowel that is healed, defunctionalized, or in a quiescent state.[80,90,91] This fact alone would preclude total colectomy as a practicable method of preventing cancer. Secondly, despite the numerous series and individual reports of the coexistence of colitis and cancer — strong evidence in favor of a relationship — we believe that the real incidence of malignancy in ulcerative colitis is much smaller than is suggested in the many articles. Very few extensive, random series have been reported, containing mild ambulatory patients as well as the severely ill and hospitalized. Lyons and Garlock[85] showed how one can vary the same sets of figures to produce different percentage results. We believe that the actual occurrence of cancer in ulcerative colitis is probably about twice the expected incidence of cancer occurring in the general population. This would make it a potential threat but not an indication, by itself, for surgical intervention. Although cancer in ulcerative colitis can be anticipated, it cannot be predicted with certainty.

Palpable Mass or Stricture

On the other hand, cancer can be hidden in the colon of a patient with ulcerative colitis and be confused with the symptoms and signs of the colitis. Therefore, any mass or stricture which cannot be reached by the sigmoidoscope for histologic evaluation must be suspected of being cancer. Too often, an infiltrating cancer of the colon or rectum has masqueraded as a benign stricture complicating ulcerative colitis. Such neoplasms are sometimes branded as being of exceptionally high malignancy with poor prognosis,[92,93] when in fact the poor outcome may have been due more to the length of time the growth went unrecognized (delay in diagnosis) rather than to any special lethal characteristic of the neoplasm itself.

In sum, irrefutable evidence is not yet available that ulcerative colitis is a precursor of carcinoma, but the overwhelming consensus subscribes to the view that cancer is more apt to develop in patients with longstanding ulcerative colitis. Large polypoid lesions or strictures developing in the course of disease should be suspected of being carcinoma.

Venereal Disease

Many of the presumed carcinogenic factors found in chronic ulcerative colitis are also discernible in venereal lymphogranuloma involving the bowel: continuous destruction of the mucosa caused by an inflammatory process with simultaneous attempts at regeneration and the accompanying stricture, particularly in the rectum. In addition, fistulization which is often present is another possible precursor to cancer. *In brief, the essential intestinal lesions consist of ulcerations; proctitis; segmental (particularly left-sided) or even universally distributed colitis; localized suppurations; anal, anoperianal, anorectal, rectoperineal or rectovaginal fistulas, and intestinal (usually rectal) strictures which may be tubular or diaphragmatic in type.*[94] The proctitis and proctocolitis, both acute and chronic, are frequently indistinguishable from nonspecific lesions. The stricture may be accompanied by fistulization or by lymphoroids (which can only be distinguished from cancer by histologic examination). The coexistence of this venereal disease with cancer of the pelvis, vulva and anorectum is apparently not fortuitous.[95] This association with malignancy is unparalleled in other venereal diseases.[96]

We have observed a number of epidermoid cancers in the rectal strictures and the various fistulas as well as adenocarcinoma above the sites of rectal strictures.

Fistulous Tracts

Chronic draining cutaneous fistulous or sinous tracts of long standing located anywhere in the body, e.g., thoracic, abdominal or osseous (osteomyelitis), have been known to be the seat of malignancy. Chronic irritation or a growth-promoting factor in inflammatory exudates is believed to be the carcinogenic cause.[97] We have observed epidermoid and colloid cancer in: (1) untreated anal fistulas as well as in fistulotomy scars; (2) suppurative hidradenitis; (3) donovanosis, and (4) venereal lymphogranuloma in the presence of rectal strictures, draining sinous tracts and/or fistulas. We have not encountered cancers in similar fistulous tracts found in association with chronic ulcerative colitis. These considerations are our motivation for more aggressive and earlier elimination of fistulous and sinous tracts whenever possible.

Recently the occurrence of cancer in draining pilonidal sinuses of long duration has been reported.[98,99]

Diverticulitis and Leucoplakia

Cancer with obstruction of the colon may precipitate inflammation in concomitant diverticula. However, at the time of this report there is still considerable uncertainty as to what extent diverticulitis is incidental or etiologically directly contributory to the infrequent occurrence of cancer in the segment of the colon involved in diverticulitis or to the still rarer occurrence of cancer within the diverticular pouch.

Leucoplakia is considered a precursor to malignancy by some authors and denied or questioned by others.

Condyloma Acuminatum

Malignant degeneration of this lesion is occasionally reported.[100] However, Young[101] in a series of studies has reported that he has never observed cancer of the rectum in the presence of condylomata acuminata (viral warts). He believes that these lesions confer an immunity against cancer in the terminal bowel in "the same manner as vaccinia protects against small pox."

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19-101. May be obtained from author or the reprints.

When some people yell for tolerance, what they really want is special privilege.
— Garner (Louisiana) Leader

"Science without religion is lame, Religion without Science is blind." — Einstein

Nonunion of the Surgical Neck of the Humerus

Method of Internal Fixation

FRACTURES OF the surgical neck of the humerus may present a problem because of difficulty in obtaining and holding a satisfactory reduction. The majority of these fractures are well treated by nonoperative methods. However, there is the occasional fracture, which has to be internally fixed initially, and others which have gone on to a nonunion, necessitating operation.

The operative treatment of these fractures with Rush pins[3] in most cases gives satisfactory results. At times, however, Rush pins do not maintain adequate reduction so that other methods have to be considered. Methods previously advocated have included circumferential wires,[4] screws,[2] and a blade plate.[1]

Patients with established nonunions of the surgical neck present a more difficult problem because of the need of secure fixation while retaining shoulder motion. A shoulder spica maintains immobilization,[5] but shoulder motion suffers during the prolonged period of immobilization. The use of a blade plate according to the method of Bosworth offers a secure method of internal fixation. However, in a nonunion, the humeral head is severely osteoporotic and there is danger that the blade will cut out of the head, if early motion is attempted. Since in nonunion cases shoulder motion is usually compromised, early motion postoperatively is a prerequisite for a good result. To combat the tendency for the blade plate to cut out of the humeral head, we modified the plate in the following manner. One inch was removed from the blade, and this end was then rounded off so that one and three-sixteenth inches of the blade remained. An oval slot, slightly larger than a three-sixteenth-inch Rush pin, was made in the blade and located just distal to the middle of the blade.

Operative Procedure

Bicortical cancellous bone strips were removed from the ilium. A Henry shoulder-strap incision was made, and the deltopectoral interval developed. The deltoid was retracted laterally, and the fracture site identified. All fibrous and synovial-like tissue between the fracture ends was removed, and the bone ends were opened by drilling.

The blade end of the plate was inserted into the humeral head below the rotator cuff

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and angulated medially and superiorly. The shaft of the plate was aligned with the humeral shaft. The extreme porosity of the humeral head enabled the blade to cut out of the head easily with abduction of the shoulder. A small incision was made through the rotator cuff, and a three-sixteenth-inch Rush pin was inserted down through the humeral head and passed through the oval slot in the blade into the distal humeral fragment. Insertion of the Rush pin through the oval slot in the blade is easy. Since the working area involved is small, the exact position of the slot is readily ascertained. (In cadavers we used small Kirschner wires to pass through the humeral head and find the slot. However, in the actual operation this was not necessary.)

After the passage of the Rush pin, the plate was then affixed to the humeral shaft with screws. Even with abduction done at the operating table, the blade plate was

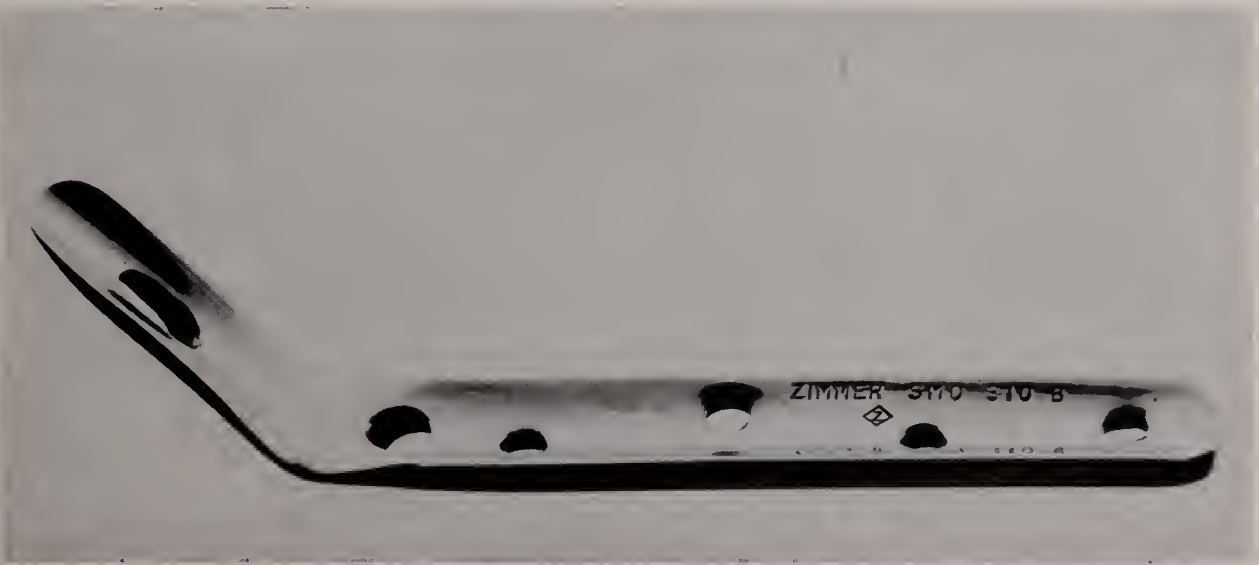


Fig. 1 — Oblique view of blade plate showing short blade and the slot cut in the blade.

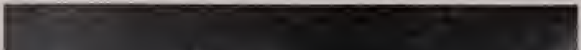
securely fixed to the head and shaft. The bone graft was applied around the fracture area, and closure of the wound was done in the usual manner. The arm was put in a sling and swathe for three weeks. Circumduction exercises were then started and the sling maintained for another two to three weeks. Free motion was then allowed.

Case Reports

Case 1.

A 59-year-old male was admitted to the hospital on December 6, 1958. Two days prior to admission he sustained a fracture of the left olecranon and distal radius, plus a comminuted fracture of the left humeral surgical neck. The olecranon was fixed internally; both it and the radius healed without subsequent difficulty. The humoral fracture was never well reduced, but was held in a posterior splint with a sling and swathe. He was started on circumduction exercises at three weeks.

Outpatient visits in February and April revealed a painful nonunion with no shoulder motion. In April a bone graft was applied along with internal fixation consisting of a modified blade plate and Rush pin. There were no postoperative complications. At three weeks he was started on circumduction exercises and left the hospital several days later against advice. He did not return until September 1959, when he presented with a solid union of the humerus, 80 degrees of abduction and no pain. Both the blade plate and Rush pin were then removed, and three months later he had 120 degrees of active abduction.



Case 2.

A 71-year-old male fractured his right humerus in January 1961. A sling was applied and discarded after several months. When first seen at the hospital on June 7, 1961, he had less than 10 degrees of shoulder abduction. A spike of the humeral shaft protruded near the coracoid process, and the shoulder was extremely painful. The humeral head could be moved freely in the glenoid. X rays disclosed a nonunion.

Operation was performed on June 13, 1961. A nearthrosis was found, and fixation plus a bone graft was applied as previously described. He was held in a sling and swathe for three weeks and then started on circumduction exercises. At five weeks the patient was allowed full use of his arm. A small stitch abscess was opened at six weeks and healed quickly. At this time the patient was free from pain and had 30 degrees of abduction. Eleven weeks after operation bony union was present both clinically and by X ray. At twelve months he had 90 degrees of active abduction with no pain. The absence of normal abduction seemed to be related to decreased muscle strength and soft tissue contracture, since the Rush pin did not impinge on any overlying bony structure when the arm was abducted.

Case 3.

A 69-year-old male fractured the surgical neck of the right humerus in August 1960. He was treated in a sling and swathe but did not return for follow-up care. In July 1961 he returned to the Minneapolis General Hospital with a painful shoulder and no active shoulder abduction. A nonunion of the surgical neck of the right humerus was seen on X ray.

Operation was performed on his right shoulder on July 7, 1961, and internal fixation plus a bone graft was applied as outlined. The postoperative course was uneventful, and by October 1961 he had 45 degrees of abduction and bony union, and he was free from pain. After twelve months he had 90 degrees of active motion. Again abduction seemed related to lack of muscle power and fibrous tissue contracture.

Comments

None of the patients have normal shoulder motion. However, with the nonunion and lack of abduction before operation, the end results appear satisfactory. Using the blade plate alone gave firm fixation of the humeral head to the shaft, and without early motion this fixation would have sufficed. With motion the blade cut out of the osteoporotic head. The Rush pin through the slotted blade stopped this, and early motion could be

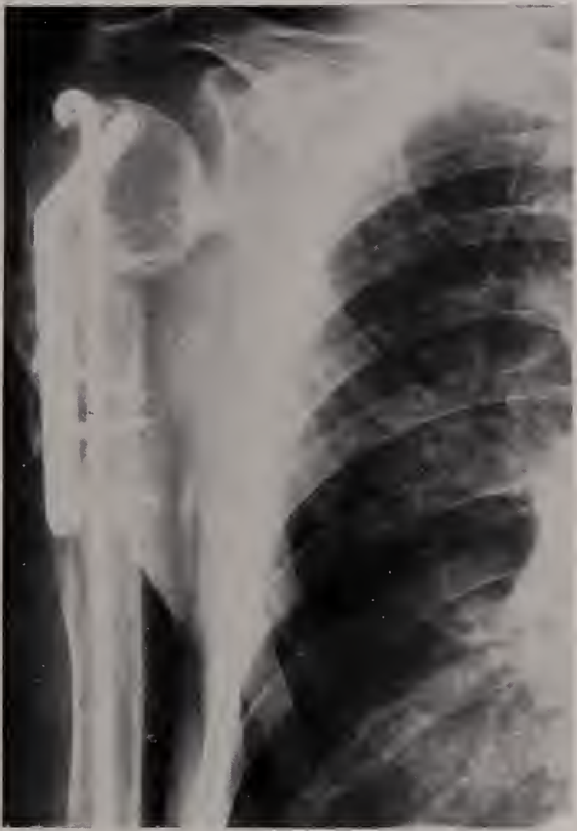


Fig. 3 — (Case 2) Roentgenogram of right shoulder made in August 1961, two months after internal fixation and bone grafting. The Rush pin is through the slot in the blade plate.

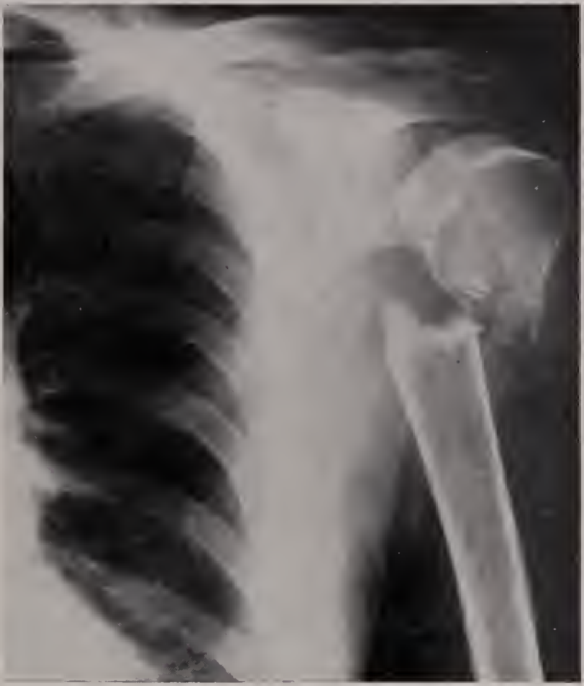


Fig. 4 — (Case 1) Roentgenogram made January 14, 1959, showing inadequately reduced left humeral neck fractures and early callous formation.

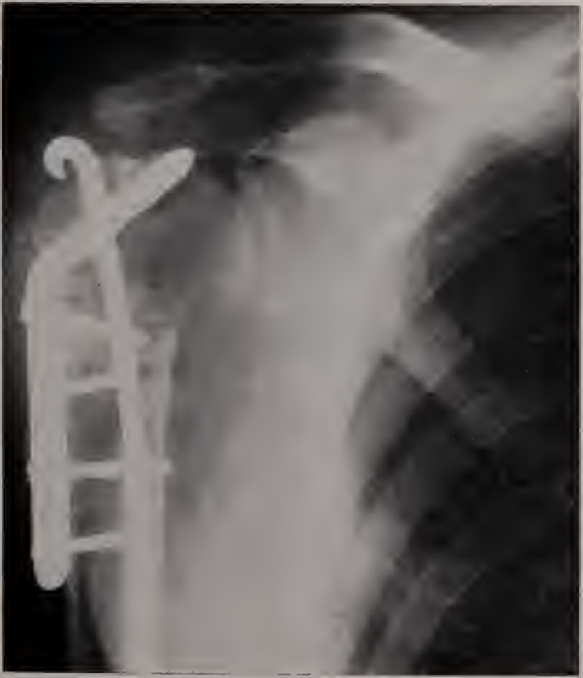


Fig. 5 — (Case 1) Roentgenogram made in June 1959, two months after operation. The blade end of the plate was too long, necessitating removal of the plate after bony union.

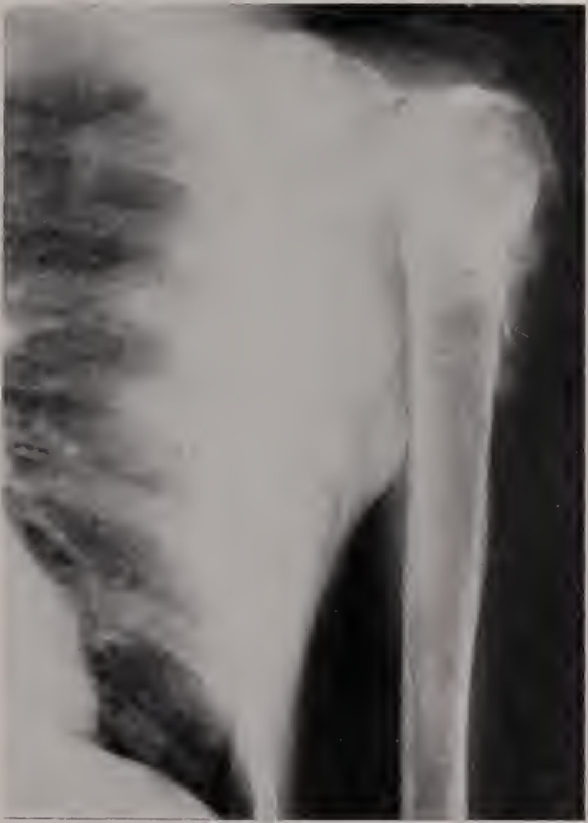


Fig. 6 — (Case 1) Roentgenogram made in October 1959, following removal of internal fixation devices. Solid bony union and good position of fragments is shown.

achieved along with bony union. The insertion of the Rush pin is technically easy and adds little time to the procedure. It is possible that late removal of the pin will aid abduction in some patients.

Summary

Three cases of nonunion of the surgical neck of the humerus are presented to illustrate a new modification of the blade-plate fixation technique. In each case solid bony union was achieved along with improvement in the range of motion at the shoulder.

NOTE: We extend our thanks to the Minneapolis Veterans Administration Brace Shop for the modification of the blade plate, and to Doctor Joseph Kiser, of the Minneapolis General Hospital, for permission to report his case.

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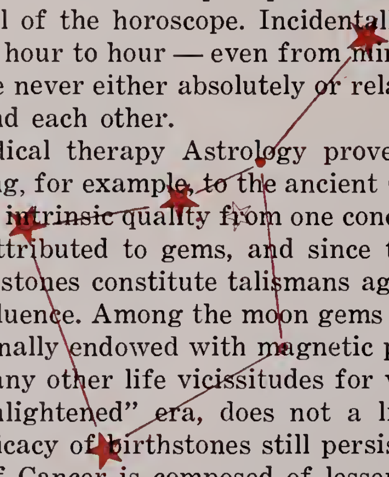
Astrology and Medicine — Cancer, the Crab

Cancer, the Crab, whose stellar configuration is here delineated, is the nativity sign for those born between June 22 and July 22, when the sun is domiciled in that constellation. Astrologically, Cancer governs the breast and gastric regions, and consequently is responsible for the health or disease of those parts — depending on the presence or absence of benefics and/or malefics, and also on the complex pattern of their mutual aspects within the total wheel of the horoscope. Incidentally, the intricate wheel pattern changes from hour to hour — even from minute to minute — since the celestial bodies are never either absolutely or relatively stationary with reference to Earth and each other.

In the field of medical therapy Astrology proves to be versatile and adaptive — subscribing, for example, to the ancient Chaldean theory of the occult transmission of intrinsic quality from one concrete object to another. Special virtues are attributed to gems, and since the ruler of Cancer is the moon, the moon's stones constitute talismans against afflictions due to adverse Cancerian influence. Among the moon gems are emeralds, crystals, and pearls — traditionally endowed with magnetic power against not only the diseases but also any other life vicissitudes for which Cancer is culpable. Even in this "enlightened" era, does not a lingering, if irrational faith in the magic efficacy of birthstones still persist?



The constellation of Cancer is composed of lesser magnitude stars and is difficult to locate in the sky, overshadowed as it is by its predecessor, Gemini, and its follower, Leo — both more brilliant and dominant. Though not dramatic, Cancer is distinctive for having nestled in one of its angles the stellar cluster, Praesaepe, popularly known as The Beehive. In spite of its relative dimness, however, Cancer, the Crab, can be identified by the patient and careful scrutinizer of the southern ecliptic during clear March evenings. A star guide of the heavens is always helpful.

The mind of the bigot is like the pupil of the eye; the more light you pour upon it, the more it will contract. — *O. W. Holmes*

Telling your troubles is swelling your troubles. — *Construction Digest*

Congenital Heart Disease

Diagnosis of*

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THE SPECTRUM of anatomical malformations in congenital heart disease ranges from an isolated obstruction or an isolated opening in a major vessel or outflow tract to a complex combination of abnormal obstructions or openings at multiple sites which may be associated with an abnormal position of the heart and/or great vessels. The type and extent of diagnostic evaluation in congenital heart disease depends in part upon the suspected complexity of the anomaly and in part upon the orientation and experience of the individuals engaged in the diagnosis. For example, in certain patients without cyanosis some institutions may rely primarily on clinical, radiographic and electrocardiographic findings. Other institutions may commonly employ additional studies such as cardiac catheterization and/or angiocardiography; the emphasis placed on these two procedures varies from place to place. Angiocardiography is becoming increasingly emphasized since it is a direct method of demonstrating pathologic anatomy and provides a qualitative visual picture of the altered hemodynamics. Such demonstrations are appreciated by the surgeons who can actually see the lesions and are a delight to radiologists whose basic interest lies in the art of demonstrating hidden structure both normal and abnormal.

As a general rule, the more clinically complex the lesion, the more useful is angiocardiography. It is the procedure of choice in cyanotic heart disease where unusual patterns of flow often preclude accurate interpretation of physiologic catheterization data.

The nature of a suspected cardiac lesion is obviously important. It may be equally important, however, for the rural practitioner to recognize the necessity of sending a child to a center for cardiac evaluation and, if so, how urgently.

The answer lies, in part, in the examination of the routine roentgenogram of the thorax.

Cardiac Enlargement

Minor degrees of cardiomegaly are difficult to appreciate. A frontal chest film exposed during expiration may reveal what appears to be a "bulky" heart. A film, exposed in the same patient during inspiration, may show the true situation of a perfectly normal-sized heart. Occasionally a large thymus gland hugging the base and the sides of the heart may mimic cardiomegaly. A close examination of the heart border will often reveal a slight prominence which represents the overlapping lower margin of the thymus.

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*Presented at the Minnesota State Medical Association Annual Meeting in Rochester, May 19, 1964.

**Assistant Clinical Professor, Department of Radiology, University of Minnesota and Director Cardiovascular Diagnostic Unit, Department of Radiology, St. Joseph's Hospital, St. Paul, Minnesota.

Failing this, a brief fluoroscopic examination during a maximal inspiratory effort at the end of a cry will reveal a decrease in the volume of tissue about the base of the heart, indicating its identity as thymus. Rarely will a mediastinal tumor closely applied to the heart give the impression of cardiomegaly.

Pulmonary Vessels

A most important part of the interpretation of the chest film has to do with the pulmonary vasculature. Four basic patterns are seen.

Increased Pulmonary Vasculature

First and most common is increased pulmonary vasculature. Anomalies associated with a left-to-right shunt and increased pulmonary flow are characterized roentgenographically by an increase in the size of the pulmonary trunk and accentuated pulmonary vasculature. The shunt may be intracardiac, as occurs, for example, in defects of the atrial or ventricular septum; or it may be extracardiac, resulting from a communication between the great vessels such as patent ductus arteriosus or aortic-pulmonic window.

All of these conditions, at some time or another, may be accompanied by or develop an increase in pulmonary vascular resistance and pulmonary hypertension. When this state is established the pulmonary trunk and central pulmonary vasculature become strikingly prominent, while the peripheral pulmonary vasculature becomes attenuated. The stage has been set for the development of a right-to-left shunt, and cyanosis may become apparent.

Certain so-called admixture lesions (obligatory bidirectional shunts), such as complete transposition, common ventricle, total anomalous pulmonary venous connection and truncus arteriosus, are characterized by increased pulmonary vasculature. Most often these patients are recognized soon after birth because of cyanosis.

Diminished Pulmonary Vessels

The second pattern, that of diminished pulmonary vasculature, is usually the direct result of obstruction to pulmonary flow. Examples of such anomalies include the tetralogy of Fallot, tricuspid atresia and pulmonary atresia.

Normal Pulmonary Vessels

The third pattern, that of normal appearing pulmonary vasculature, occurs in those conditions associated with obstructions on the left side of the heart, for example: aortic stenosis, coarctation, and fibroelastosis. When these anomalies are severe, pulmonary congestive changes may appear.

Obstruction to Inflow

The fourth pattern of the pulmonary vasculature is seen in those conditions characterized by obstruction to the inflow of pulmonary venous blood. Cor triatriatum,* obstruction of the pulmonary veins and congenital mitral stenosis may cause a diffuse increase in the density of both lung fields or a fine, central, pulmonary streaking with poor definition of individual vascular markings.

Alteration of Cardiovascular Contour

As a general rule abnormal positions of the heart (dextroversion and dextrocardia) are associated with other cardiac anomalies, and often the prognosis is poor.

Normally the left cardiovascular silhouette is formed from above downward by the aortic knob, the pulmonary trunk and the left ventricle. The right silhouette is formed by the superior vena cava above, and the right atrium below.

The subtle variations in contour are as numerous as the types of congenital heart lesions. There are, however, some bold alterations which are diagnostically significant. The most obvious of these are the result of a change in size or position of the great vessels.

Ventricular Septal Defects

Enlargement of a great vessel is usually the direct result of either increased flow or partial obstruction; an opinion as to which of these states is responsible must necessarily be based on the appearance of the pulmonary vasculature. This is particularly true in the case of the pulmonary trunk. For example, in ventricular septal defect and left-to-right shunt there may be obvious enlargement of the pulmonary trunk; the presence of increased pulmonary vasculature suggests that the enlargement is due to increased flow. When ventricular septal defect is associated with pulmonary hypertension there is often striking enlargement of the pulmonary trunk, caused in this instance by a combination of increased flow and an element of obstruction, the latter resulting from an elevated pulmonary resistance secondary to occlusive changes in the pulmonary vascular bed.

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*See Test Your Word Score Page 359.

Pulmonary Stenosis

In severe pulmonary stenosis the pulmonary trunk may become very large. In this situation, however, the mechanism is different. The dilatation results from turbulence and abnormal pressures on the wall of the pulmonary trunk distal to the valvular stenosis — so-called poststenotic dilatation. In such a case the pulmonary vasculature may be diminished,, suggesting that the cause of the enlargement is one of partial obstruction to flow.

Tetralogy of Fallot

Aortic enlargement in the presence of diminished pulmonary vasculature usually indicates the presence of obstruction to pulmonary flow in association with a right-to-left shunt at either the atrial or ventricular level. The common example in this category is the tetralogy of Fallot. Less common anomalies showing somewhat similar features are pulmonary atresia and tricuspid atresia.

Congenital Valvular Aortic Stenosis

Obvious enlargement of the ascending aorta in the presence of normal-appearing pulmonary vasculature should arouse suspicion of a left-sided lesion. A common anomaly of an obstructive nature causing poststenotic dilatation of the aorta is congenital valvular aortic stenosis.

Diminished size of the great vessels may on occasion result in an alteration of cardiovascular contour. Detection of such, however, is often impossible in the infant because the vessels are frequently obscured by the thymus. Once the thymus gland undergoes involution, decreased size of the outflow portion of the right ventricle and pulmonary trunk, as occurs, for example, in the tetralogy of Fallot, will result in a distinct concavity of the upper mid-portion of the left cardiovascular silhouette. Detection of diminished aortic size in roentgenograms of the thorax is very difficult, if not impossible.

Malposition of the Great Vessels

Finally, malposition of the great vessels may result in contour alteration. For example, those cases of complete transposition with an anteroposterior relationship of the great vessels will show a narrow cardiac "waist." In corrected transposition the aorta arises anteriorly from the base of the heart on the left side. The pulmonary trunk is medially located.

Summary

When the information from a careful radiologic examination of the heart, great vessels and pulmonary vasculature is combined with the clinical findings, a big step may be taken toward the diagnosis and a very important decision can be made concerning the disposal of the patient.

Obviously cyanotic patients require an early, definitive diagnosis to separate the potentially correctable from the noncorrectable case.

On the other end of the spectrum is the noncyanotic patient with a murmur, but with absent or minimal radiologic signs and no disturbing clinical signs such as: decreased exercise tolerance, poor weight gain, intermittent pulmonary infections and cardiac decompensation. In this situation there is usually no urgency for cardiac evaluation. Observation, periodic radiologic and electrocardiographic examinations will often show no sign of change, and additional studies may be deferred until the child is older.

In contrast, an aggressive attitude is best when in noncyanotic patients there are signs of developing pulmonary hypertension, since this is the main factor which determines operability and ultimate prognosis. The two most important observations, short of cardiac catheterization, which will suggest the presence of pulmonary hypertension, can be made with the use of the stethescope and the roentgenogram. An increase in loudness and snapping of the pulmonary second sound in concert with increasing size of the pulmonary trunk and central pulmonary vasculature accompanies this undesirable development.

The same aggressive attitude should pertain when in children signs of cardiac failure appear; not uncommonly the underlying cause is a correctable, obstructive left-sided malformation.

SHEEHAN'S SYNDROME

(Postpartum pituitary necrosis)

Panhypopituitarism is due to postpartum thrombosis of sinuses and ischemic infarction and necrosis of the pituitary gland. It is suggested that the syndrome occurs much more frequently than is generally recognized. If a woman suffers a severe hemorrhage, collapse, or shock at the time of delivery or during the early postpartum period, she should be observed closely for subsequent signs of pituitary necrosis. The symptoms of this condition are multiglandular, some showing myxedema. There is pallor, asthenia, apathy, atrophy of the breasts with loss of areolar pigment, inhibition of lactation, loss of public and axillary hair, and genital atrophy. Amenorrhea may be temporary or permanent. Diabetes mellitus, if present, vanishes. Hypoglycemia is usually found and may be sufficiently severe to produce coma. A flat glucose tolerance curve and extreme sensitivity to insulin may be demonstrated.

There is a reduction in the excretion of the corticoids in the urine and when both the anterior and posterior lobes of the pituitary have been involved, there may be a marked diminution in the gonadotropins, thyrotropins, and corticotropins accounting for the descriptive term "panhypopituitarism."

Treatment should be directed to polyglandular administration. If potent, dependable pituitary extract is not available, then cortisone or hydrocortisone with dersecated thyroid and estrogen replacement will give varying results from satisfactory to excellent.

Durham—Encyclopedia of Medical Syndromes—Haeber Inc. New York.

The Penalty of Overweight

In autopsy studies it has been demonstrated that there is a close association between obesity and atherosclerosis with advanced degrees of arterial changes being found twice as often among the obese as among the poorly nourished individuals.

— Cyril M. McBryde, M.D., Signs & Symptoms, Lippincott Co.

Speak well of your enemies; remember you made them. — This Month

The Natural History of Cholelithiasis

*A 15 to 30-Year Follow-up of 116 Patients**

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DESPITE THE voluminous literature on disease of the gallbladder there is no uniformity of opinion concerning the advisability of cholecystectomy in the patient with gallstones. Recommendations range from operation on all patients with cholelithiasis, on the assumption that "there are no innocent gallstones," to operation on only those with troublesome symptoms or complications.

In an attempt to determine what our advice to patients with cholelithiasis should be we have collected information on a group of patients who for any reason did not have cholecystectomy at or near the time gallstones were discovered and who have been followed for 15 or more years after diagnosis or until death. By so doing we have hoped to shed some light on the natural history of cholelithiasis.

Selection of Patients

From the files of the Mayo Clinic for the years 1930 through 1945 we obtained information on consecutive patients who had cholelithiasis but did not undergo cholecystectomy during the clinic admission in which that diagnosis was made. No diagnosis of cholelithiasis was accepted unless gallstones had been visualized by radiography or had been palpated at operation for another condition. We excluded those patients in whom cholecystectomy was performed as the result of the original medical advice, even though that operation was initially deferred, unless the patient returned because of additional symptoms. We chose only those patients with a local address (Rochester, Minnesota) in order to eliminate the selectivity of referred patients.

TABLE I
Cholelithiasis: Status of 116 Patients Not Operated on at Time of Diagnosis

Age at time of diagnosis, years	Patients	Symptoms at time of diagnosis			Operation deferred by physician
		None	Indigestion only	Colic	
18	1	0	1	0	0
20-29	8	0	0	8	0
30-39	18	3	4	11*	0
40-49	25	3	7	15	5
50-59	26	1	6	19	7
60-69	24	4	8	12	6
70-79	11	2	3	6	4
80-89	3	1	2	0	3
Total	116	14	31	71	25(22%)

*Associated acute pancreatitis.

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*Read at the meeting of the Southern Minnesota Medical Association, Mankato, Minnesota, September 10, 1964.

**Section of Medicine, Mayo Clinic and Mayo Foundation.

Records of 132 patients meeting these requirements were obtained, and in 116 (88 per cent) of these we were able to acquire adequate information concerning the subsequent course until death of the patient or for 15 or more years after the diagnosis had been made. Of these 116 patients, 104 were females and 12 were males.

Results

One hundred two of the 116 patients with cholelithiasis were *symptomatic (88 per cent)* at the time of diagnosis and 71 (70 per cent) of these had had pain. Only 14 (12 per cent) could have been considered as having "silent" gallstones (Table 1). Age distribution at the time of diagnosis followed an anticipated pattern with 93 of the 116 cases of gallstones being discovered in the *fourth through seventh decades of life (80 per cent)*. In 25 cases *surgical treatment was considered inadvisable (22 per cent)* because of other illness, obesity or old age. No attempt was made to evaluate in each of the other cases the degree to which the need for operation was emphasized to the patient, although it was evident that this varied widely among the physicians involved.

Table 2 summarizes the status of the 116 patients followed for 15 or more years subsequent to the diagnosis of cholelithiasis or until death. At the conclusion of the study 63 patients were still living and 53 had died. Fifty-nine of the total number had had an *operation on the gallbladder (51 per cent)*, 56 of them because of symptoms attributed to gallbladder disease, two because cholecystectomy was indicated and feasible at the time of other intra-abdominal operations, and one for unknown indications. For any one decade of life in which gallstones were discovered the percentage of patients eventually having an operation roughly paralleled the life expectancy for that age. Of the 27 patients with cholelithiasis discovered when the patient was less than 40 years of age, 23 had cholecystectomy before termination of the follow-up-period (85 per cent); of the 52 patients less than 50 years of age, 38 eventually had an operation (73 per cent), and of the 78 patients less than 60 years of age, 52 underwent operation (67 per cent).

Fifty-seven of the 116 patients had not been *operated on by the end of the follow-up period (49 per cent)*, but seven of these were having persistent severe symptoms (Table

TABLE 2
Cholelithiasis: Status of 116 Initially Unoperated Patients
After 15 to 30 Years

Age at time of diagnosis, years	Patients	Status at follow-up	Required operation on gallbladder		Severe symptoms	Deaths and cause
			Number	Per cent		
18	1	Living 1	1	100		
		Dead 0				
20-29	8	Living 8	8	100		
		Dead 0				
30-39	18	Living 17	13	76		
		Dead 1	1			
40-49	25	Living 18	12	60	1	
		Dead 7	3			
50-59	26	Living 13	9	54	2	1 (carcinoma of gallbladder)
		Dead 13	5			
60-69	24	Living 6	4	25	2	1 (rupture of gallbladder)
		Dead 18	2			
70-79	11	Living 0		9	2	1 (carcinoma of gallbladder)
		Dead 11	1			
80-89	3	Living 0		0		
		Dead 3	0			
Total	116	Living 63	59	51	7	3(3%)
		Dead 53				

3). Of the 14 patients who were asymptomatic at the time of diagnosis, 10 remained asymptomatic and two required surgical treatment eventually; but of the 102 patients who were originally symptomatic 57 (56 per cent) eventually had had an operation, most of them because of severe symptoms. Ten of the 26 patients with cholelithiasis whose gallstones had been discovered when the patients were less than 60 years of age, but who had not had gallbladder surgery, were having varying degrees of indigestion or pain or both up until death or the end of the follow-up period, but in only three of these were symptoms severe and frequent. Of the 25 patients who were advised not to have surgical treatment because of ill health, marked obesity or old age, only two eventually required it.

None of the patients in this series died as a result of surgical treatment. Three died as the direct result of gallbladder disease: two because of carcinoma of the gallbladder and one because of rupture of the gallbladder.

TABLE 3
Cholelithiasis: Final Symptomatic Status of 116 Patients Not Operated on at Time of Diagnosis

		Status on follow-up	
Symptoms at time of diagnosis	Patients	Remained unoperated	Persistent severe symptoms
Asymptomatic	14	12	1
Indigestion only	31	19	3
Pain	71	26	3
Total	116	57	7

Discussion

Observations in large post-mortem series have shown the incidence of gallstones to be about 10 per cent in all people more than 20 years of age and about 30 per cent in white females and 15 per cent in white males in the seventh decade of life, with less than half that incidence seen among Negroes.[1-6] Physicians have been finding only a small proportion of these during life. If we really believe that gallstones carry a high risk, then we should be surveying the general population beyond the age of 40 or 50 years and advising all of those with gallstones, whose health permits, to have cholecystectomy. Obviously we have not been doing this, probably because it seems unrealistic either to obtain cholecystograms or to consider cholecystectomy in such large numbers. The universal result is that cholecystograms are usually obtained only when symptoms suggest that disease of the gallbladder may be present.

Indications for Surgery in Patients With Symptoms

There is quite uniform agreement that all patients with gallstones who have associated serious complications such as jaundice, acute cholecystitis or pancreatitis should be operated on. Most of us will agree that the patient with repeated attacks of colic or troublesome indigestion or both, which can be presumed to be associated with his gallbladder disease, should be advised to have cholecystectomy if his health permits. From this study it seems obvious that the younger the patient when symptoms lead to the diagnosis of gallstones, the more likely it is that he will eventually require surgical treatment. Of those less than 60 years of age when the diagnosis of gallstones was established, 67 per cent eventually required an operation on the gallbladder, and there was an abrupt drop in the percentage requiring an operation when the diagnosis was made after that age. It therefore seems reasonable to advise cholecystectomy in the patient less than 60 years old with symptomatic gallstones. In those more than 60 or 65 years of age we believe that the decision concerning operation must be individualized.

Our main area of indecision remains, as it has since the beginning of this century, in what to advise the patient with silent gallstones or whose gallbladder disease has caused only mild symptoms or a single episode of colic.

Indications for Surgery Without Symptoms

There has accumulated considerable statistical information which adds great weight to the opinion that all gallstones should be removed when they are found. For example, Enderlin[7] in a large post-mortem series found that 40 per cent of those with gallstones had complications from them and that these complications were the cause of death in 8.7 per cent and were contributory causes in 7.8 per cent. Post-mortem studies have also shown a 4 to 5 per cent incidence of carcinoma of the gallbladder in patients with gallstones beyond the age of 60 years, although clinical series including all age groups in recent years show an incidence closer to 0.5 per cent.[8-10] Mortality rates for cholecystectomy increase with age, particularly in the over 65 group, and complications such as acute cholecystitis, pancreatitis and jaundice cause a manyfold increase in risk even in the best of hands. Comfort and colleagues[11] in a 10 to 20-year follow-up of 112 patients with silent gallstones that had been discovered at operation for other conditions found that 51 had developed symptoms and that 24 of these had required cholecystectomy, with three deaths postoperatively.

Although these representative figures from the literature would encourage us to consider cholecystectomy in asymptomatic cholelithiasis, Robertson's[12] words of caution in 1945 are still worth listening to: *"to advocate an operation on every gallbladder that is found to contain gallstones is so drastic a recommendation that it would appear reasonable for the proponents of this advice to reexamine the premises on which it is based."* It is not enough to point out that a sizable percentage of patients with asymptomatic gallstones will eventually require an operation, that the risk of operation increases with age and with complications, or that a significant number will die as the result of gallbladder disease, especially in old age. It is necessary to be able to compare the risk of operation in a group of patients with asymptomatic gallstones at a given age with the risk in that same group in which a certain percentage of patients unoperated on for gallstones will later either become symptomatic and/or develop complications that require surgical treatment with increased risk. It would also seem advisable to be able to calculate the man-years of life expectancy lost because of the surgical mortality in asymptomatic gallstones and compare this with the man-years lost if surgical treatment is deferred until it becomes mandatory or until disease of the gallbladder causes death.

Surgical Mortality

To search out all people who have gallstones means that each individual would require multiple cholecystograms during his lifetime. A prerequisite to operation on all those who develop gallstones would be a lower mortality rate for cholecystectomy than the anticipated mortality rate for disease of the gallbladder as it is handled in this country at present. The Metropolitan Life Insurance Company lists the average annual death rate for diseases of the gallbladder as 3.8 per 100,000 for both white men and women aged 35 to 74 in the period 1960-1962;[13] this means that an individual aged 45 years with a life expectancy of 30 years stands a 0.11 per cent chance of death from gallbladder disease before age 75. If the combined average incidence of gallstones in white men and women at age 45 is 10 per cent, then the risk of death from gallbladder disease in patients with gallstones and a 30-year life expectancy is about 1 per cent. The surgical mortality in uncomplicated cholelithiasis should be no more than half of this. Whether these calculations would have differed significantly if only patients with asymptomatic gallstones had been considered is a matter only for conjecture. However, Lund[14] concluded, in his series of patients with gallstones who were not treated surgically and were followed for five to 20 years after diagnosis, that the prognosis for those with asymptomatic stones was not much better than that for patients with other types of the disease.

Nevertheless, the figures available suggest that not more than one out of every four or five patients with gallstones will ever require surgical treatment for them,[11,14,15] and that therefore a four or fivefold mortality rate in the 20 to 25 per cent of patients eventually requiring an operation would not exceed the total mortality rate if all patients with asymptomatic gallstones had been operated on. Unfortunately, there are no large long-term studies available on people with asymptomatic gallstones to show the comparative risks.

Morbidity in Lost Man-years

We have been speaking only of mortality rates without taking into consideration the age at which death occurs. We should include in our calculations the risk rate in terms of man-years lost because of surgical mortality at the time asymptomatic gallstones are discovered and contrast this with the surgical risk rate at a later age when some of those same gallstones have become symptomatic and some complicated, adding to this the death rate from gallbladder disease itself. For example, in terms of man-years lost, the surgical loss of a young patient with 40 years of life expectancy would equal the loss of four older patients each with 10 years of life expectancy. In this connection it is well to recognize that if we are to advise surgical treatment for silent gallstones, the total man-years lost by operating during a low-risk situation may outweigh that by delaying operation until it becomes necessary. The greatest risks in gallbladder disease are in old age when surgical risks increase and carcinoma of the gallbladder develops, but it is also then that life expectancy is least.

A corollary to this is an intangible factor which no figures can answer. This pertains to the value of a year of life at various ages. For example, we believe all would agree that the value of a year to a woman in her 40s with a family might be greater than a year in her 60s when her children have been educated and are self-sufficient. If this be true, it is an added factor in avoiding operation at a time when a currently benign condition is asymptomatic.

There are certain situations in which we believe that cholecystectomy in the patient with asymptomatic gallstones should be seriously considered: (1) when the gallbladder is nonfunctioning on cholecystography; Clagett[16] found that 27 per cent of a series of 150 such patients who originally refused operation were forced to undergo one for serious complications such as jaundice, pancreatitis and perforated gallbladder within two years after the diagnosis had been made; (2) when gallstones are present in a patient with a troublesome duodenal ulcer; (3) when abdominal exploration is undertaken for another condition and cholecystectomy is feasible without undue increase in risk; and (4) probably when multiple small stones are demonstrable.

The search for gallstones in the general population, even if confined to limited age groups, would be expensive and time-consuming and would require the conviction of all physicians that cholecystectomy in asymptomatic cholelithiasis is not only justified but imperative. Cholecystectomy even when uncomplicated would necessarily result in small but significant morbidity and mortality rates in a relatively young, asymptomatic, productive and active segment of the population and unfortunately would leave some individuals with unpleasant postoperative symptoms. We do not believe that there is as yet certain statistical evidence which makes cholecystectomy advisable in the asymptomatic patient with gallstones, nor do we believe that a routine search for gallstones is a realistic undertaking at present.

Conclusions

The younger the age at which gallstones are discovered the greater is the probability that cholecystectomy will become necessary eventually. In this reported series of patients with gallstones, two thirds of those less than 60 years of age when the diagnosis was established required surgical treatment later.

All patients less than 60 years of age who have gallstones with significant associated symptoms should have an operation if general health permits.

After the age of 60 years the likelihood that cholecystectomy will be necessary before death occurs from a cause other than gallbladder disease, is sharply reduced, and therefore the decision concerning operation should be individualized.

Mortality rates should be calculated in terms of man-years of life expectancy lost when the advisability of cholecystectomy for silent gallstones is considered.

The decision concerning cholecystectomy in patients with asymptomatic gallstones remains unsettled except for a few specific indications, which are listed. We believe that the routine search for asymptomatic gallstones and cholecystectomy in all patients in whom they are discovered is unjustified at present.

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WHAT'S YOUR DIAGNOSIS?

A 64-year-old white male patient had a stroke about five years prior to hospital admission with residual aphasia and paralysis of the left upper extremity. Three weeks prior to his admission he had suddenly started having painless jaundice, associated with "coca-cola" colored urine. His relatives had not observed the color of his stools. His temperature was normal throughout this period. His relatives denied that he had any previous history of weight loss or any abdominal discomfort. No food intolerance was noted. The patient was a diabetic, controlled with Orinase. He had been admitted to another hospital with diagnosis of viral hepatitis and subsequently transferred here.

Physical Examination: The patient was a well-nourished white male with aphasia and with paralysis of the upper right extremity; he was jaundiced but not in acute distress. The abdomen was very slightly distended. Liver and spleen were not palpable. No tenderness was found. No tumors were felt. The rest of the physical examination was essentially negative.

Pulse 92, regular. Blood pressure 110/80. Temperature 99.5, orally. Respiration Rate, 24/min., regular.

Laboratory Work-up: Prothrombin Time, 15 sec. Transaminase: 140, Glucose, 158; Bilirubin Total 21.8, direct 18.9. Thymol Turbidity, 1.2. units; Alkaline Phosphatase 21.5 King Armstrong unit, Urine Urobilinogen 0, repeated .46. An upper G. I. series was reported, normal.

Hospital Course: The patient's condition did not change. His jaundice stayed about the same clinically. On the seventh day after his admission, he was taken to surgery.

What's your Diagnosis? Turn to page 337.

Results of Cholecystostomy in the Treatment of Acute Cholecystitis

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For some medical complications and technical hazards cholecystostomy is a helpful procedure.

CHOLECYSTOSTOMY IS not a new method for the treatment of gallbladder disease.[1] During the last 15 years there have been numerous reports describing its use in various biliary tract conditions.[2-5] The present report concerns the use of cholecystostomy for acute cholecystitis alone, with particular emphasis on the medical and technical indications for the choice of this procedure.

For this study, the records of all patients treated surgically for acute cholecystitis at the Mayo Clinic in the 7-year period from January, 1951, through December, 1957, were reviewed. Particular emphasis was placed on the indications for and results of cholecystostomy in this group. The clinical diagnosis of acute cholecystitis was confirmed in each case by the findings at operation and, in some cases, by review of pathologic material removed at operation.

During this 7-year period, 7769 operations were performed for chronic cholecystitis and 446 for acute cholecystitis. In the latter group, 62 patients (14 per cent) underwent cholecystostomy. For the purposes of our study, this latter group was then divided into operations performed for medical indications (29 cases) and those performed for technical indications (33 cases). Follow-up information on each patient was obtained either by subsequent examination or follow-up letters.

Cholecystostomy for Medical Indications

Twenty-nine of the 62 cholecystostomies were performed for medical indications. This represents 47 per cent of the cholecystostomies done for acute cholecystitis during the 7-year period. The ages of these patients ranged from 32 to 91 years (average, 66

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years). Fifteen were men (average age, 71 years) and 14 were women (average age, 61 years). One patient had undergone cholecystostomy 28 years prior to cholecystostomy at the Mayo Clinic for recurrent acute cholecystitis.

Not only were the associated medical conditions varied, but, in most instances, the presence of multiple medical problems precluded more definitive surgical treatment (Table 1). The most frequent disorders were extreme obesity, marked coronary artery disease, severe hypertension, and advanced cerebrovascular insufficiency. Fourteen of the 29 cholecystostomies were performed as planned procedures with local anesthesia.

TABLE 1
Medical Indications for Cholecystostomy

Indication	Patients*
Extreme obesity	12
Marked coronary artery disease	11
Severe hypertension	9
Advanced cerebrovascular insufficiency	6
Rheumatic heart disease	4
Diabetes mellitus	3
Previous myocardial infarct	2
Severe toxicity	2
Emphysema	2
Asthma	1
Carcinoma of the pancreas	1
Carcinoma of the prostate	1
Myxedema	1
Squamous cell carcinoma of the lung	1
Severe burn	1
Rhabdomyosarcoma of the scapula	1

*Some patients had more than one indication.

Multiple stones were removed from the gallbladder in 20 cases; a single stone was removed in seven cases and in two cases no stones were recovered. In one case, choledochostomy was performed in association with cholecystostomy with removal of a common duct stone.

Period of Convalescence

The duration of postoperative hospital convalescence ranged from nine to 66 days (average, 21 days). Postoperative complications included asthmatic attacks (two cases), atelectasis (one case), superficial thrombophlebitis (one case), cardiac arrhythmia (three cases), and exacerbation of rheumatic heart disease (one case). There were five postoperative hospital deaths, an operative mortality of 17 per cent (Table 2).

TABLE 2
Hospital Deaths After Cholecystostomy for Medical Indications

Age	Sex	Postop. day	Cause of death
82	F	40	Anemia and azotemia
32	F	41	Cirrhosis
68	F	48	Carcinoma of pancreas
44	F	14	Electrolyte imbalance
79	M	31	Bilateral pulmonary emboli

Follow-up information was available in 22 of the 24 patients who survived operation (92 per cent). The duration of follow-up ranged from three months to 12 years (average, 3½ years). Fifteen of the 22 patients traced had not experienced recurrent biliary symptoms. Six of these asymptomatic patients survived for two to 12 years following operation, and nine died of associated medical disease within five years after operation. Three others died with no information available concerning biliary symptoms.

Incidence of Recurrent Symptoms

Three patients underwent subsequent cholecystectomy for recurrent symptoms six months to two and one-half years after the cholecystostomy; one of these patients died of carcinoma of the gallbladder three and one-half years after the initial operation.

If we include under "symptomatic patients" those who underwent cholecystectomy at a later date, those who died with no information available regarding biliary symptoms, and the patient who died of carcinoma of the gallbladder, the incidence of recurrent symptoms after cholecystostomy for medical indications was 32 per cent.

Cholecystostomy for Technical Indications

Thirty-three of the 62 cholecystostomies were performed for technical indications. This represents 53 per cent of the cholecystostomies done for acute cholecystitis during the 7-year period. The ages of these patients ranged from 35 to 86 years (average, 63 years). Twenty-one were men (average age, 66 years) and 12 were women (average age, 61 years). One patient had had two previous cholecystostomies, performed 29 and 31 years prior to treatment at the Mayo Clinic.

The major disease states that contraindicated cholecystectomy in the medical group were, for the most part, present in this group also, but less frequently and to a lesser degree of severity. Patients in this group underwent surgical exploration that was expected to lead to definitive surgical treatment for acute cholecystitis. However, at operation it was found that the degree of inflammatory reaction had so obscured and distorted the normal anatomic landmarks that the surgeon thought that attempts to remove the gallbladder would be associated with a serious risk of injury to the common duct or other portal structures; thus cholecystostomy was performed.

Multiple stones were removed from the gallbladder in 30 cases, a single stone was removed in two cases, and no stone was recovered in one case. In two patients, choledochostomy was performed in association with cholecystostomy, with removal of common duct stones in each instance.

Period of Convalescence

Convalescence was considerably shorter in this group than in those in whom cholecystostomy was performed for medical reasons; the duration of postoperative hospital convalescence ranged from eight to 30 days (average, 14 days). Postoperative complications included one instance each of wound evisceration, thrombophlebitis, acute epididymitis, atelectasis, multiple pulmonary emboli, and cerebrovascular accident. There was only one death in the immediate postoperative period, an operative mortality of 3 per cent. This patient was an 83-year-old man who died on the twenty-sixth postoperative day after progressive development of confusion.

Follow-up information was available in 27 of the 32 patients who survived operation (85 per cent). The duration of follow-up ranged from two months to 11 years (average, six years). Fifteen of the 27 patients traced had not experienced recurrent biliary symptoms. Eleven of the asymptomatic patients survived from four to 10 years after operation; four patients died of intercurrent disease from one to 10 years after operation. One patient died seven years postoperatively but no information was available concerning biliary symptoms. Two patients were alive with recurrent biliary symptoms eight and 11 years, respectively, after operation.

Incidence of Recurrent Symptoms

Nine patients have undergone subsequent cholecystectomy. One patient had a planned interval cholecystectomy six months after the initial operation. Two patients had their gallbladders removed as part of another operative procedure eight and 11 years following cholecystostomy; in neither case had there been recurrent biliary symptoms. In six cases cholecystectomy was performed for recurrent symptoms two months to nine years following cholecystostomy. In two of these six cases, stones were removed from the common duct at exploration.

If we include under "symptomatic patients" those who subsequently underwent cholecystectomy, those patients who died with no information available regarding biliary symptoms, and those alive with recurrent symptoms, the incidence of recurrent symptoms after cholecystostomy for technical indications is 44 per cent.

Discussion

Among operations performed for acute cholecystitis, cholecystostomy has comprised from 3.7 to 28 per cent[6-9] and was 14 per cent in the present series.

The group that had the operation for medical indications had a somewhat older average age than that of the group that had the operation for technical indications. Also, the average age of these patients was approximately 10 years older than that of the patients in a similar series reported earlier from this institution.[4]

The severity of the associated disease in the group in which cholecystostomy was performed for medical indications is suggested by the higher mortality, both early and late, as compared to that group in which cholecystostomy was performed solely for technical indications. The over-all operative mortality of 9.7 per cent is consistent with that of previous reports.[5,6,8] However, it should be noted that, of the eight deaths following 446 operations for acute cholecystitis, six occurred in the 62 patients undergoing cholecystostomy; 14 of the procedures were performed as planned cholecystostomies. The use of the planned cholecystostomy was recently discussed thoroughly by Sparkman.[10]

The incidence of recurrent biliary tract symptoms after cholecystostomy in the present group of patients was 39 per cent, which is considerably lower than incidences reported by others.[3,5] In both of our groups, symptoms frequently recurred a few months postoperatively, and, in two cases, cholecystectomy was performed for recurrent difficulty as long as nine years after the initial operation. Two patients had recurrent acute cholecystitis 28 and 31 years after cholecystostomy. In addition to the possibility of late recurrence of symptoms, it should be noted that even those patients who had severe medical conditions when operated on frequently had prolonged survival following cholecystostomy. In view of these facts, it would seem important to consider additional and more definitive surgical treatment for all patients undergoing cholecystostomy, to be done when their general condition permits. There were no postoperative deaths in any of the patients who had subsequent cholecystectomy in this series. However, it was disappointing to note how few patients subsequently underwent elective interval cholecystectomy.

It is apparent from this discussion that cholecystostomy is not the treatment of choice for acute cholecystitis. It is not without risk and is associated with a high incidence of recurrent symptoms. Yet, in the severely ill patient with acute cholecystitis complicating associated difficult medical conditions or in the patient operated on for acute cholecystitis in whom more definitive procedures are contraindicated for technical reasons, cholecystostomy seems to offer reasonable palliation. Experience indicates that cholecystostomy has no virtues over more definitive procedures when the latter can be accomplished expeditiously and in a technically satisfactory manner. In dealing with the individual patients it is obvious that many factors must be considered in electing operative intervention and in choosing the procedure to be employed. The safest and most definitive procedure should be selected within the limitation imposed by circumstances.

Conclusions

Cholecystectomy is the safest and most definitive procedure in the majority of cases of acute cholecystitis. Although only a palliative procedure, cholecystostomy has definite value in the treatment of some patients with acute cholecystitis.

When performed for technical reasons or because of the presence of associated severe disease conditions, use of this operation does not indicate surgical timidity but good surgical judgment.

In the patient who is acutely ill with associated medical disease, planned cholecystostomy may be a lifesaving procedure if more definitive procedures cannot be accomplished expeditiously and in a technically satisfactory manner.

Unless contraindicated by other conditions, all patients who have had cholecystostomy should be considered for delayed elective cholecystectomy, since otherwise many will have subsequent difficulties.

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Pliny's* Cure for Earache

For pains and diseases of the ears Pliny recommended using the urine of a wild boar, kept in a glass vessel, or the gall of a wild boar, swine, or ox, mixed with castor oil and oil of roses in equal proportions. The best remedy for earache, however, was the bull's gall, warmed with leek juice or with honey, and this was particularly effective if there was some suppuration.

For offensive exhalations from the ears, the bull's gall, warmed in a pomegranate rind, was considered to be very excellent. "Some persons are of the opinion that it is a good plan to wash the ears with this preparation in cases where the hearing is affected; while others again, after washing the ears with warm water, insert a mixture composed of the old slough** of a serpent and vinegar, wrapped up in a dossil of wool."

In all cases where there is any rupture of the ear drum, these preparations are used in combination with woman's milk.

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*See Minnesota Medicine June 1964, Page 716.

**Slough — the cast off skin.

ANSWER TO WHAT'S YOUR DIAGNOSIS

(From page 332)

A laparatomy with common bile-duct exploration revealed one single stone in the common bile duct, close to the ampulla. The common bile duct was thick and fibrotic, while the gallbladder was found to be small and atrophic, showing evidence of a previous inflammatory process. A cholecystectomy was done. Following surgical intervention the patient has had an uneventful postoperative recovery with clearing of his jaundice.

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Dr. John H. Finley stated that all people who came to him in trouble for counsel he advised these three courses of action: Take a long walk; read a good book; make a new friend. — York Trade Compositor

The man who cannot think is less than man; the man who will not think is traitor to himself; the man who fears to think is superstition's slave. — Robert Ingersoll

*The size of your troubles generally depends on whether they are coming or going.
— Sunshine Magazine*

Opportunity knocks on the door but once. Trouble is more persistent — Banking

Gastrointestinal Hemorrhage

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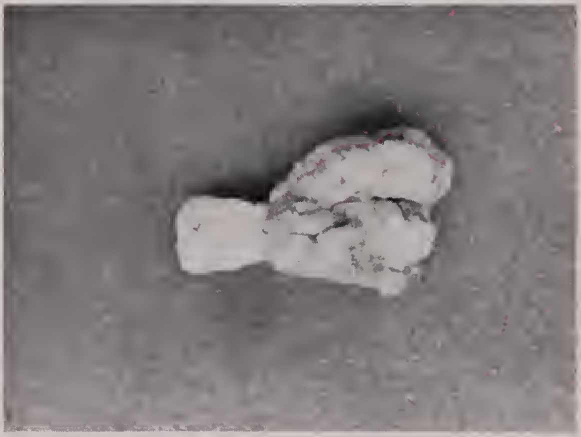

Fig. 1 — Adenomatous polyp of jejunum

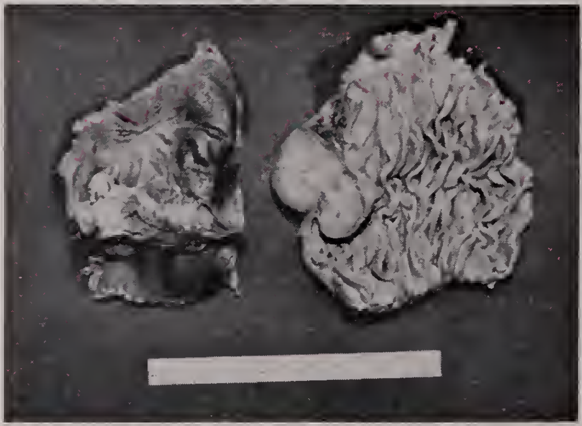

Fig. 2 — Neurilemmoma of jejunum

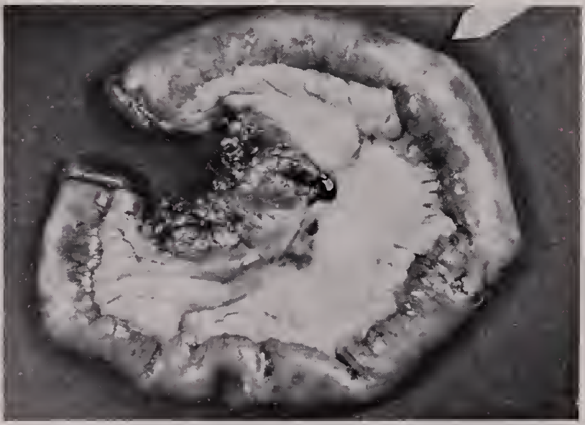

Fig. 3 — Segment of ileum containing three carcinoids. Mesenteric lymph nodes are involved.

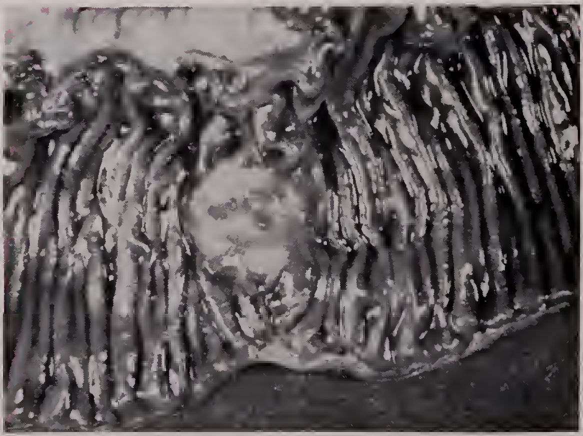

Fig. 4 — Ulceration of mucosa of ileum by a carcinoid.

from Lesions of the Small Intestine

Report of Six Cases

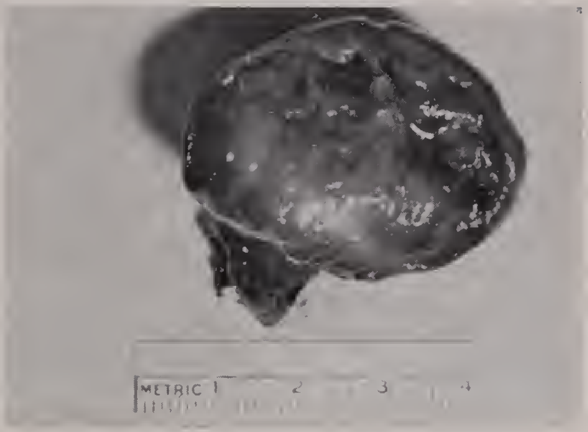

Fig. 5 — Polypoid adenoma of duodenum

Bleeding into the gastrointestinal tract continues to present a serious problem which taxes our resources in arriving at a correct diagnosis and in instituting proper treatment. In the majority of cases gastrointestinal hemorrhage is correctly attributed to lesions of the esophagus, stomach, duodenum, or colon, areas in which diagnostic procedures are accurate and fairly easily carried out. In a significant number of cases the site of the hemorrhage cannot be determined by the diagnostic methods now available.

Although it is generally stated that hemorrhage from the small bowel is uncommon, a careful consideration of this area as a source of bleeding will probably produce a better yield of bleeding lesions. There has been a tendency to neglect the jejunum and ileum in diagnostic considerations in determining the source of gastrointestinal bleeding. Diagnosis is difficult because of the length of the small bowel, its mobility, the elasticity of the bowel wall, and the relatively small size of the lesions.

From the records of a large hospital, embracing a forty-nine year period, Brief and Botsford[1] have recently reported a series of sixteen cases of major bleeding from the mesenteric parts of the small intestine. The lesions included eight neoplasms, three primary nonpeptic ulcers of the jejunum, and one case of each of the following: Meckel's diverticulum, diverticulosis, telangiectasis, blind-pouch syndrome, and granuloma secondary to Witzel's enterostomy. Although this small number of cases from this sophisticated center seems to indicate that primary bleeding from the small bowel is rare, I believe that this is misleading and that hemorrhagic lesions in the small bowel are more common than has been suspected.

During the past eight years, in a small hospital, I have observed and treated five patients who were bleeding from lesions of the mesenteric small bowel and one additional patient who had hemorrhage from a polyp of the duodenum. Hemorrhage, or related symptoms, such as anemia, inability to keep the blood at a satisfactory level, weakness, dyspnea, etc., were the major complaints. Not any of the patients had hematemesis, although it has been shown[2] that hematemesis can occur when the bleeding lesion is below the ligament of Treitz. Two of the patients were known to have duodenal ulcers; preoperatively it was thought that the bleeding originated in these ulcers.

In none of the patients was the source of the bleeding determined before operation. Two of the patients had been extensively studied in prominent medical centers where every diagnostic tool was available.

Adenomatous Polyp of Jejunum

A white female, age 43 years, was admitted to the hospital on May 12, 1958, because of weakness, anemia, and black stools of one week's duration. She had been weak and "all in" for a year. In 1955, when she had become weak and dyspneic, she was treated elsewhere with transfusions, but the source of the bleeding was not determined. Several episodes of gastrointestinal bleeding followed with similar inability to find the source.

Except for pallor, there were no significant findings on physical examination. The hemoglobin was 6.25 grams. An irritable duodenal cap was reported; otherwise, Roentgen studies of the stomach, small bowel, and colon were reported as negative.

At laparotomy, after a very careful search, a tumor was palpated in the upper portion of the jejunum. Through an incision in the bowel wall a polypoid tumor on a long pedicle was removed. Convalescence was uneventful and the patient has remained well.

The polyp measured 1.7 x 1.4 cm. Microscopically there was found a fibrous connective tissue core with large blood vessels covered with folded, normal-appearing intestinal mucosa.

Neurilemmoma of Jejunum

A white man, age 78 years, was admitted to the hospital on November 4, 1958, because of gastrointestinal hemorrhage, anemia, and weakness. During each of his four previous admissions with the same symptoms he was given transfusions and medical treatment. A duodenal ulcer had been found on X-ray examination. Operation had been suggested but not urged because of the patient's advanced age and obesity.

At operation on November 10, 1958, a deformity and scarring of the duodenum were found. At approximately twenty-four inches below the ligament of Treitz a tumor the size of a golf ball was discovered in the jejunum. The mesenteric lymph nodes were not enlarged. Following resection of the segment of bowel containing the tumor, convalescence was smooth and complete. The patient, now age 83 years, is well.

The specimen consisted of 15 cm. of the upper jejunum. In the mid-portion of the resected specimen, adjacent to the mesentery, there was a round, elevated mass covered with smooth serosa and measuring 3 x 3 x 2 cm. The mass protruding into the lumen of the bowel measured 2.5 x 2 x 1.5 cm., and was covered with flattened mucosa showing a small area of ulceration. Microscopically the tumor was composed of irregular, large and small bundles of cells with long, narrow nuclei tending to arrange themselves in palisades. There was no evidence of malignancy.

Carcinoid of the Ileum

A girl, age 18 years, was admitted to the hospital on March 19, 1955, because of bleeding from the bowel and weakness.

In 1951, at the age of 14 years, this patient had experienced her first gastrointestinal hemorrhage. In January, 1955, there was a second episode of bleeding, followed by a third in February, 1955. Many studies had failed to disclose the source of the blood loss.

At operation a carcinoid tumor was found in the ileum three inches proximal to the ileocecal valve. Three and six inches above this tumor there were smaller carcinoids. There was also glandular involvement. The segment of ileum containing these three lesions, with the adjacent gland-containing mesentery, was excised.

The specimen consisted of approximately 60 cm. of small bowel and mesentery. There were multiple carcinoids of the ileum with ulceration and with metastasis to the mesentery and a regional node.

Since her recovery from the operation this patient has had two children and has remained well.

This patient, 18 years of age, was younger than any reported by Moertel, Sauer, Dockerty, and Baggenstoss[3] in their series of 209 cases. They found the extremes of age to be 24 and 90 years. They noted a "striking tendency toward multicentricity of origin" of the carcinoid tumor, which was a feature of the case herein reported, and in only two cases was there ulceration of the mucosal covering. They stated that gastrointestinal bleeding was not common and usually occurred late in the course of the disease.

Hemangioma of the Ileum[4]

Known to have a duodenal ulcer and while under treatment for this ulcer, a white man of 50 years was admitted to the hospital on August 11, 1957, with bleeding from the gastrointestinal tract and with weakness and fainting. He was in mild shock. Hemoglobin was 9.45 grams and the hematocrit was 28. There was no vomiting.

When the bleeding did not cease, operation was performed on August 15. The stomach and upper small bowel were free of blood. In the mid-ileum there was an area in which the blood vessels beneath the serosa were dilated; there was also thickening of the bowel wall. This segment of bowel was resected and was found to contain a hemangioma from which the patient was bleeding. Recovery was prompt and permanent.

The presence of blood in the lumen of the bowel below the lesion and the absence of blood above the lesion were of great help in locating the origin of the hemorrhage.

Polyp of Duodenum

An elderly white male, age 79 years, had a hemorrhage from his intestine in the spring of 1962. During his hospitalization elsewhere he was given transfusions, and a diagnosis of duodenal ulcer was made.

In early December, 1962, the patient became weak and dyspneic. When he was found to be anemic he was again hospitalized, transfused, and studied; but his hemaglobin continued to fall.

On December 27, 1962, this patient was admitted to Naeve Hospital. He was well preserved and pale; his stool was black. The hemoglobin was 9.5 grams. Roentgenologic examination did not disclose the source of the bleeding. Normal value for hemoglobin was restored by transfusions, but it fell slowly and occult blood was present in the stools.

At exploration on January 16, 1963, examination of the stomach, duodenum, small bowel, and colon did not disclose any abnormalities. Cardiac arrest occurred during this exploration but normal sinus rhythm was promptly restored.

The duodenum was opened. In the retroperitoneal portion of the duodenum a tumor was palpated and subsequently delivered into the wound and removed. It measured 4 cm. in diameter; one surface was flattened and ulcerated. The stalk was 2 cm. in length and 1 cm. in diameter. The pathology report was ulcerated polypoid adenoma of Brunner's glands.

Unfortunately the patient remained drowsy following the operation and his temperature soared to 104°. He expired on January 18. Although permission for autopsy was not obtained, it was thought that he sustained cerebral damage during the cardiac arrest.

According to Charles, Kelley, and Campeti,[5] most primary duodenal tumors are benign and are located in the first portion of the duodenum, in contrast to the patient herein reported in whom the polypoid adenoma was in the third portion. Twenty-one of the thirty-one tumors reported by these authors were benign and only two, a cyst and a lymphangioma, were in the second portion of the duodenum. Only five of the patients had tumor bleeding.

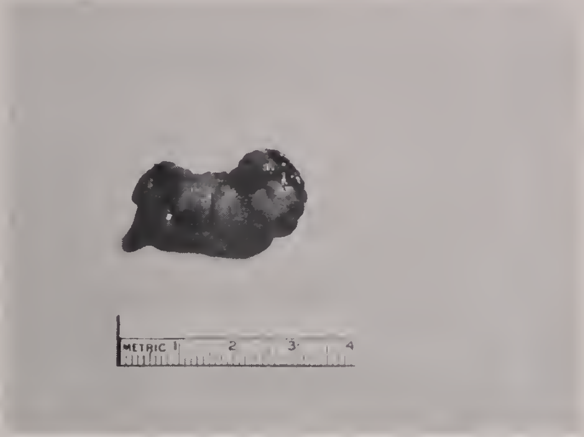

Fig. 6 — Polypoid leiomyoma of ileum

Polyp of Ileum (Leiomyoma)

A white man, age 47 years, gave a long history of intestinal hemorrhage which began in 1956 when he had his first hemorrhage. Examinations were negative. He remained well for two and one-half years.

In 1959 there was a severe hemorrhage which necessitated transfusions. Examinations were again negative. The patient was told that he had iron deficiency.

In 1960 there was another hemorrhage from the bowel and more transfusions. The bleeding was thought to be on the basis of capillary fragility.

From May, 1962, to March, 1963, this patient was in the hospital nine times and was transfused each time. He stated that he had spent more than four thousand dollars for medical expenses during this period.

On March 18, 1963, the stools became black and numerous, and the patient was admitted to Naeve

TABLE I

Hemorrhagic Lesions of Small Bowel

Lesion	Location	Age of Patient	Sex	Internal From First Symptom to Surgery	Result
1. Adenomatous Polyp	Jejunum	43	Fe	3 Years	Well
2. Neurilemoma	Jejunum	78	M	1 Year	Well
3. Carcinoid	Ileum	18	Fe	4 Years	Well
4. Hemangioma	Ileum	50	M	4 Days	Well
5. Adenomatous Polyp	Duodenum	79	M	9 Months	Died
6. Leiomyoma	Ileum	47	M	7 Years	Well

Hospital on March 19 in mild shock. Hemoglobin was 6.7 grams. Thirteen units of blood were administered during this hospitalization. Roentgenologic examination was again negative except for "spasm" of the duodenum.

At exploration on March 27, a polyp in the midileum was promptly found and removed. The tip of this polyp was 1.6 cm. in diameter, with ulceration of two thirds of its surface. The stalk was 2 cm. in length and 1.1 cm. in diameter. The pathologic diagnosis was ulcerated polyp, probably on the basis of a pedunculated leiomyoma.

Pfister and Tatarowicz[6] estimate that in fifteen per cent of cases of gastrointestinal hemorrhage the origin of the bleeding remains obscure. Retzloff, Hagedom, and Bartholomew[7] found that exploratory laparotomy in 100 cases of gastrointestinal hemorrhage of obscure origin revealed the site and cause of the hemorrhage in 30 patients, of whom 12 had lesions of the small bowel. If there is persistence or recurrence of the bleeding and its source eludes detection by available diagnostic procedures, laparotomy is indicated. This should consist of meticulous examination of the entire gastrointestinal tract with opening of the stomach or duodenum when necessary. After their discovery, small bowel lesions are usually not difficult to excise surgically.

Summary

In gastrointestinal hemorrhage of obscure origin, either gross or occult, consideration should be given to lesions of the small bowel. In most instances these lesions cannot be detected prior to exploratory laparotomy. Here presented are six cases of gastrointestinal hemorrhage from small bowel lesions, all of which were found at laparotomy and all amenable to surgical treatment. One elderly patient succumbed to cerebral damage caused by cardiac arrest; five patients are well.

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Australopithecus*

It is not, of course, that you have entirely failed to acquire specializations. You have a moderately outsized head, and thoroughly outsized buttocks. Also, you have flat feet, a chin, and an embarrassing lack of fur. But a zoologist visiting from some distant planet, having overcome his first repugnance for a mammal almost as hairless as a hippopotamus, will probably not be unduly fascinated by your head-size. Enlargement of the brain is a primate, not just human, characteristic. What will enthrall him will be the magnificent development of the human buttocks and the peculiar specialization of the feet. — African Genesis — Robert Ardrey

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*See Minnesota Med Feb. 1965, p. 169.

I honestly believe it is better to know nothing than to know what ain't so.
— Josh Billings

Resolve to perform what you ought; perform without fail what you resolve.
— Benjamin Franklin

Acute Emphysematous Cholecystitis[**]

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ACUTE EMPHYSEMATOUS cholecystitis is an inflammation of the gallbladder associated with gas-forming organisms. Stoltz first reported gas in the gallbladder in 1901. His findings were on autopsy cases, and he thought the emphysema was a post-mortem occurrence.[1] Lobinger, in 1908, was the first to describe gas in the gallbladder at surgery.[2] VonFriedrich, in 1929, described the X-ray appearance of emphysematous cholecystitis, and Hegner, in 1931, made a preoperative diagnosis on the basis of the X-ray appearance of the gallbladder.[3] Although at least 105 cases have been reported in the medical literature, only seven of these were reported prior to 1940.[1,4]

Etiology

The etiologic mechanism of emphysematous cholecystitis is not completely understood. Just as in other cases of cholecystitis, there is an obstructive mechanism, usually a stone in the cystic duct. Over 50% of the patients give a past history of symptoms consistent with gallbladder disease.[5] About one-fourth of the patients with emphysematous cholecystitis are *diabetic.*[6] An interesting paradox is the fact that, whereas in all cases of cholecystitis, approximately 80% of the cases are females, in emphysematous cholecystitis the situation is reversed with approximately 83% of the cases occurring in men.[7] *This high incidence in males has never been explained.*

Organisms found in cases of emphysematous cholecystitis are all normal inhabitants of the gastrointestinal tract. *Clostridium welchii and Escherichia coli* have been cultured in 19 out of 50 gallbladders characterized by emphysematous cholecystitis.[7] Anaerobic streptococci and staphylococci are also cultured in some cases of this disease. It is interesting that these organisms are also commonly found in gallbladders submitted for pathologic examination in which there was no evidence of emphysematous cholecystitis.[8] Gordon-Taylor and Whitby found them in 19 out of 100 specimens submitted after surgery for chronic cholecystitis.[9] Markowitz has shown that even normal, healthy livers of adult dogs frequently harbor Clostridium welchii.[10] Andrews, Rewbridge, and Hrdina demonstrated that if the contents of the gallbladder of a dog were drained into its pelvis or thoracic cavity, severe gas gangrene developed. These authors concluded that there was a primary hepatitis with direct extension to the gallbladder. They demonstrated that the strains of

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Clostridium welchii commonly isolated from the gallbladder of man at operations for cholecystitis and from the gallbladders of healthy dogs are of very low virulence as well as being non-spore-forming.[10]

It would seem that, in order for these gas-forming organisms of low virulence to grow, there must occur a markedly lowered resistance of the tissues. Gordon-Taylor and Whitby state that intestinal bacteria are the organisms most frequently found in gallbladder infections. They have noted that Clostridium welchii is usually associated with acute forms of cholecystitis. In nearly 9% of a series of gallbladders removed at surgery, they were able to isolate this organism and found it in the center of 13% of gallstones obtained in the post-mortem room. They concluded that the most reasonable anatomical explanation for infection of the gallbladder is the passage of intestinal bacteria via the portal system to the liver and then through the periportal lymphatics to the gallbladder. The observation of Andrews and his associates, that in acute cholecystitis that portion of the gallbladder adjacent to the liver is more edematous and thickened, would tend to support this theory.

Diagnosis

The diagnosis in emphysematous cholecystitis is dependent upon an X-ray picture of gas in the gallbladder (Fig. 1). One of the interesting phenomena seen in an X ray of an emphysematous gallbladder is a ring of gas surrounding the gas within the lumen of the gallbladder. This linear outline of gas surrounding the lumen of the gallbladder is apparently caused by perforation of gas through the mucosa into the submucosa where it dissects around between the submucosa and the muscularis of the gallbladder.[6] Following this, with increasing pressure, the gallbladder may rupture with the development of pericholecystic abscesses. Indeed, the presence of a pericholecystic abscess has been found in 71% of patients with emphysematous cholecystitis.[6]

Differential Diagnosis

Other than this fairly typical X-ray picture, the symptoms in acute emphysematous cholecystitis are quite typical of acute cholecystitis in general, being somewhat more acute and severe in nature. Having demonstrated gas in the gallbladder, there are four other conditions which might be considered:

1. An internal biliary fistula. In this condition gas is also seen in the biliary radicals, whereas this is not true in emphysematous cholecystitis. In addition there is no gas in the wall of the gallbladder in patients with an internal biliary fistula. Moreover, the communication with the gastrointestinal tract may be demonstrated in these patients by a barium meal or by barium enema examination.

2. Incompetence of the sphincter of Oddi may result in gas within the gallbladder, but the ducts will also contain gas.

3. Lipomatosis of the gallbladder. The radiolucency of lipomatous tissue may simulate gas in the gallbladder. However, there is no fluid level as there is in emphysematous cholecystitis and no change in the configuration of the translucent shadow with a change of position.

4. Gallstones may contain gas, but the X-ray picture is quite different from that of emphysematous cholecystitis. The gas in gallstones produces multiple stellate radiolucencies seen in the gallbladder area.[12]

The appearance of a severe fulminating case of cholecystitis in a male, especially if

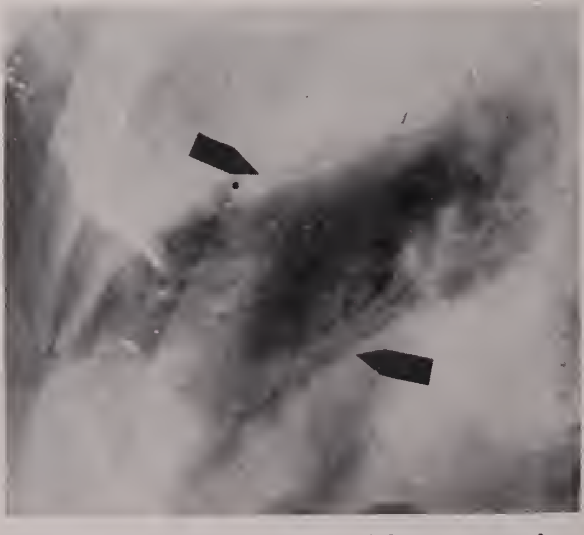

Fig. 1 — Roentgenogram of right upper quadrant of the abdomen in emphysematous cholecystitis. Arrows point to gas which has dissected around in a submucosal plane.

he is diabetic, should alert one to the possibility of acute emphysematous cholecystitis.

Treatment

There has been considerable controversy over the proper method of treating these patients. Earlier authors advocated conservative treatment, whereas recently there has been a tendency to prefer surgery, especially if the patient is seen early in the course of the disease.[5,13-15] The earlier reports demonstrated that conservative treatment carried less mortality, whereas later reports have indicated lesser mortality with surgical treatment. It is possible with antibiotic therapy to treat these patients conservatively, but the course is necessarily a long one. After subsidence of the process, the patient can be sent home and return for cholecystectomy approximately six weeks later. *However, if the patient is seen within three days of the onset of symptoms, almost all authors would prefer to treat the patient with cholecystectomy.*

Some have advocated treatment with gas-gangrene antitoxin, but no one has proved that this is of any benefit. Certainly many patients have been treated successfully without the utilization of gas-gangrene antitoxin.

Even if the patient is treated medically, the surgeon must be ready to operate at any time, as complications are frequent. The most common complications are rupture of the gallbladder and the development of pericholecystic abscesses or generalized peritonitis.

Case Report

A 76-year-old male diabetic entered the hospital on 12-10-58. His diabetes was of nine years' duration and was controlled with 20 units of N.P.H. and 40 units of regular insulin taken each morning. For three weeks he had had intermittent nausea, vomiting, and diarrhea. His condition had worsened considerably during the hours prior to admission. Abdominal pain had first been noted on the day of admission, and there was some radiation of this pain to the right scapular area. Physical examination revealed a pale, white male. There was tenderness in the right costovertebral angle, and the liver was palpable approximately two to three fingerbreadths below the costal margin. There was no abdominal tenderness, and normal bowel tones were present. A provisional diagnosis was made of diabetes mellitus with acidosis and impending coma, cholecystitis, and pyelitis. The patient was treated by vigorous control of his diabetes and parenteral administration of chloramphenicol. In addition, intravenous fluids were started. Penicillin, in dosages of 600,000 units I.M., was given every twelve hours.

Despite vigorous medical therapy the patient's condition worsened. An abdominal X ray taken on the sixth hospital day revealed gas in the gallbladder (Fig. 1). The following day, because of progressive deterioration in the patient's condition, surgery was performed. A gangrenous, emphysematous gallbladder was excised. A large pericholecystic abscess and considerable enlargement and scarring of the liver were noted. The entire upper portion of the abdomen had become walled off so as to form one huge abscess containing approximately one liter of green pus. Surprisingly, we could not culture any organisms from this pus. The wall of the gallbladder was crepitant and contained minute submucosal air bubbles two to three millimeters in diameter. The cystic duct contained several stones. The entire gallbladder floated when placed in formalin. Following surgery, the patient made an uneventful recovery and was discharged on the sixth postoperative day.

Summary

In this case, although surgery was not performed until seven days after the onset of abdominal pain and four weeks after the onset of vomiting and diarrhea, it appeared that without surgery the patient probably would have died.

Emphysematous cholecystitis should be considered whenever one is presented with a male patient who has symptoms of acute and fulminating cholecystitis, especially if diabetes is also present.

Although these patients can be treated medically, cholecystectomy is associated with lower mortality and morbidity.

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If you have knowledge, let others light their candles at it. — Margaret Fuller

The Place of Jesus in the History of Medicine

IN TRACING the rise of modern medicine the figure of Jesus is given little if any place. The justification for this exclusion seems obvious. Jesus, it is argued, was involved in healings, but his healings were unrelated to the techniques of medicine. He was a miracle worker whose importance is to be evaluated from the standpoint of religion rather than of medicine. However, such a judgment overlooks important historical facts, because it starts from a misunderstanding of the factors giving rise to modern medicine, the development of which has generally been related to the application of the scientific method. Without the use of scientific techniques in the study of the natural world and supremely in the study of man the armamentarium of the modern physician against disease would be reduced to the vanishing point. The rise of science in western civilization since the Renaissance, and especially its refinements in the last century, have brought the treatment of illness to a level ot success unparalleled in the history of mankind. But to stop the investigation of modern medicine with this statement is to fail to ask a vital question. What were the roots of that attitude of concern for the ill person which made the search for cure such an all-consuming passion?

Modern medicine is an amalgam of scientific knowledge and concern for man's wholeness. Without both these factors the rise of modern medicine would have been impossible. It would be wrong to assume that there has always been an attitude of concern for the ill. Instead, they were often shunned by others and left to their own devices until they recovered or died. Unable to bear their share of work and responsibility they were despised as worthless. In the religions of antiquity the deity sought the pure and sound as his worshippers. The sick and sinful — these were often equated — were prey to the powers of darkness and hence allowed no place in the realm of the healthy. With the exception of the healing cult of Aesculapius, the dominant belief in antiquity was that the gods rejected the ill. When the sick person recovered wholeness of soul and body, then he would again be acceptable to the gods. Celsus, the Roman philosopher of the second century, gibed the Christians for the sheer irrationality of their religion because they did not shun but rather invited the sick in mind and body to their worship.

Such negative attitudes toward illness were also common among the ancient Jews. Although by the first century there had been some modification of the earlier Old Testament attitude toward illness, the dominant view persisted that illness was a divine judgment on sin. Hence to seek to heal disease was an act bordering on impiety. Some rabbinic teachers allowed the use of medicines, even while holding that illness was divine judgment. (*Mishna*, Berakhoth, 5:3). But such teachers tended to be the exception rather than the rule; they heralded a new outlook that was soon to dawn. Most men took the attitude of Job's friends Bildad, Zophar, and Eliphaz, who when they came to comfort him amidst his grief and acute illness, kept admonishing him to search his conscience for some unadmitted sin, for surely sin was at the root of his suffering. Although the book of Job sets out to refute this overly simple equation between sin and suffering, it was a critique little understood or accepted in its time. There was to be found in neither classical antiquity nor ancient Judaism that attitude of concern for man in illness and suffering which is a basic ingredient in the growth of modern medicine. The advent of an all-embracing concern for the sick was to await the rise of a new spiritual force in western civilization: a new force to be released through Jesus and his earliest followers.

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(To be continued in April issue)

The reason why worry kills more people than work is that more people worry than work. — Robert Frost

Painful Stump Neuroma

- Treatment
- of

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Tribute to Dr. Peyton

Dr. William Peyton served as Director of Neurosurgery at the University of Minnesota from July 1, 1940, to June 30, 1960. Following his retirement in 1960, he accepted the position of attending neurosurgeon at the Minneapolis General Hospital. This post he diligently served until his death on March 3, 1962.*

Dr. Peyton was the epitome of the ideal surgeon to the residents during that time. No calls to Dr. Peyton went unanswered. Willingly and with enthusiasm, he would return to the hospital at any hour of the night to patiently instruct and supervise the resident through a delicate neurosurgical procedure. He made regular ward teaching rounds during which he would spend a considerable amount of time defining not only procedures but the pathophysiological reasons for each procedure.

He also made many suggestions to those of us on the general surgical service, one of which was responsible for the successful outcome of the case presented in the following article. Dr. Peyton will be remembered and revered as a skillful surgeon, dedicated teacher, and valued friend.

Following division of a peripheral nerve during the course of an amputation, there is a subsequent enlargement of the cut end which consists of a branching mass of Schwann cells and proliferating axones. This is termed a neuroma and is usually nontender. However, on occasion, it will become quite sensitive and be the source of a great deal of consternation to the amputee. It is not known why these neuromas are sensitive in only a few cases; however, it is thought that a poorly healed stump with excessive scarring around the nerve ending will favor the development of such a problem.

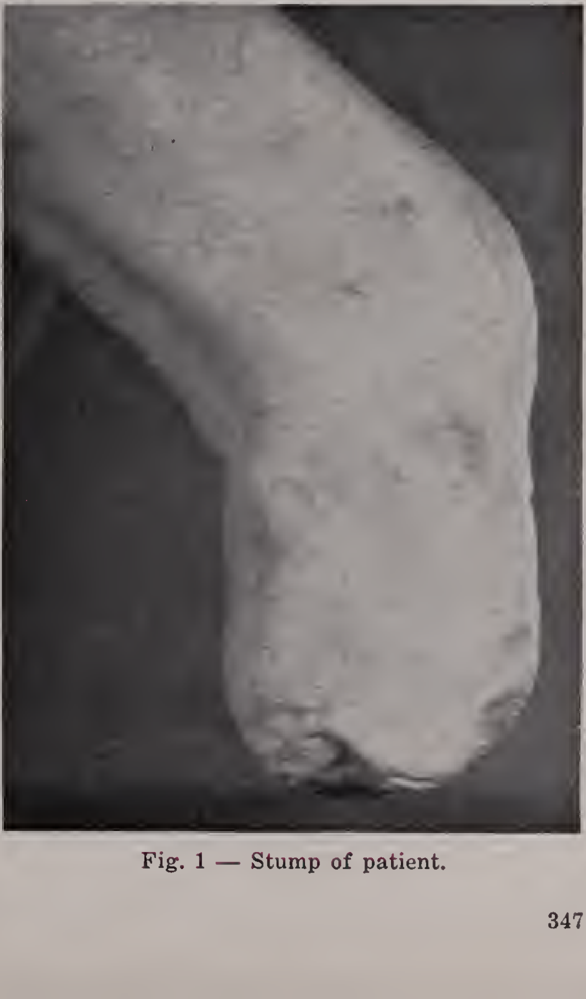

Fig. 1 — Stump of patient.

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*(Since January 1, 1964, the Hennepin County General Hospital.)

The multiplicity of problems that may develop following an amputation was well brought out and studied by S. Weir Mitchell from his extensive experience during the American Civil War.[1] In his text he states that in his observations on the stumps he studied at the 400-bed hospital for nervous diseases at Philadelphia, neuromata developed at the transected ends of all the nerves.[2]

During the course of World War II, several large-scale conferences on the problems of amputees were held and it was the consensus of opinion that if a particularly tender area of the stump is involved and if this can be temporarily ameliorated by a direct injection of 1 percent Procaine, it is fairly certain that a painful neuroma exists. During the course of one of these conferences, it was pointed out that the following procedures should not be performed for a painful stump: 1) repeated resections of neuromas, 2) neurectomies of nerve trunks at higher levels, 3) reamputation, 4) periarterial sympathectomy, 5) intrathecal injection of alcohol, 6) posterior rhizotomy.[3]

For local burning pain and tenderness which are confined to the actual stump, they recommended: 1) chemical or surgical interruption of the regional sympathetics, 2) section of the spinothalamic tract, 3) single resection of neuroma if such is located.[4]

Leriche described transecting a painful nerve trunk with immediate suture to prevent neuroma formation without striking results.[5] Boldey recommended implantation of the transected nerve into a tunnel in adjacent bone to prevent neuroma formation.[6]

At the present time, from the experience gained from World War II, it is generally recommended that the proper method for dividing large nerves during clean amputations is to first draw them down slightly, cut across them cleanly, and allow them to retract. If a central vessel bleeds, it can be ligated with fine silk.

The treatment for painful neuromas, then, is by no means standardized. Once excised, they tend to recur and dissection through a well-healed stump may lead to other undesirable results (i.e., causalgia,* scarring).

The following case history is of interest because the patient fits well the category of recurrent painful stump neuroma and because a variation of Leriche's technique proposed by Dr. Peyton led to a most satisfactory result.

Case History

A 52-year-old male was admitted to Minneapolis General Hospital in January 1955 for treatment of ischemic signs and symptoms in his right leg. It was felt at that time that the arteriosclerotic occlusive disease in the vessels of the leg was too far advanced to lend itself to a reconstructive procedure but that a lumbar sympathectomy should be performed. This was accomplished, but in the subsequent postoperative weeks, there was a worsening of the ischemic changes and in late February 1955, a below the knee amputation was performed (Figure 1).

Approximately four months after this procedure, the patient noticed the gradual onset of pain in the amputation stump. He had previously noted phantom limb pain, but this was different in that there was point tenderness in one localized area of the stump. The pain did not abate, and in January of 1958 the stump site was revised and a neuroma of the tibial nerve was excised.

The patient was pain-free for a period of three to four months and then noticed the return of his old pain. He bore the distress for a period of a year but then came back for further help. At that time deep to the mid-portion of the scar and just behind and medial to the tibia was an area of extreme sensitivity. It was felt that this lay directly over the tibial nerve ending, and after noting the pain could temporarily be relieved by direct injection of 1% Procaine, surgery was again recommended.

At surgery, a neuroma, 2 cm. wide and 4 cm. long was carefully delineated from the surrounding scar tissue. Proximal to this, the nerve was of normal size. A complete transection through the nerve just proximal to the neuroma was made and carefully reconstructed with interrupted 5-0 silk sutures. Then, 1 cm. proximal to the sutured anastomosis, a second complete transection was made and this again sutured. A third transection was planned but not performed because of a problem with exposure. The neuroma was left undisturbed and the wound closed.

Following the operation, the patient noted complete relief of pain in the stump. He has been followed for five years, has remained pain free and uses his below-the-knee prosthesis with dexterity. There has been no recurrence of his previous symptoms during the four-year follow-up.

Discussion

Dr. Peyton felt that it was the snarl of regrowing axones that acted as the trigger mechanism for the pain. If three serial transections of the nerve were made, only a small number of axones would reach the final nerve ending because of the decreasing percentage that successfully bridge each anastomosis.

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*See Test Your Word Score Page 359.

In the operation performed, it would not have been necessary to reopen the amputation site, and in fact, by so doing, the exposure was compromised and only two of the desired three transections were made. If the occasion should present itself in a different patient, an approach through the distal popliteal space would be used as diagrammed (Figure 2).

It is realized that a single successfully treated case certainly does not warrant the conclusion that all painful stump neuromas should be treated in this manner. Nevertheless, certain factors were present that made the case of definite interest: the fact that excision of the first painful neuroma failed with redevelopment of a second painful neuroma and because the second neuroma was left undisturbed in the stump. Dr. Peyton had used the procedure with success in several other patients.[7] Evaluation of a significant series of patients who have undergone this procedure at the University of Minnesota should help determine the ultimate merit of the procedure.[8]

Summary

A case of recurrent painful stump neuro-

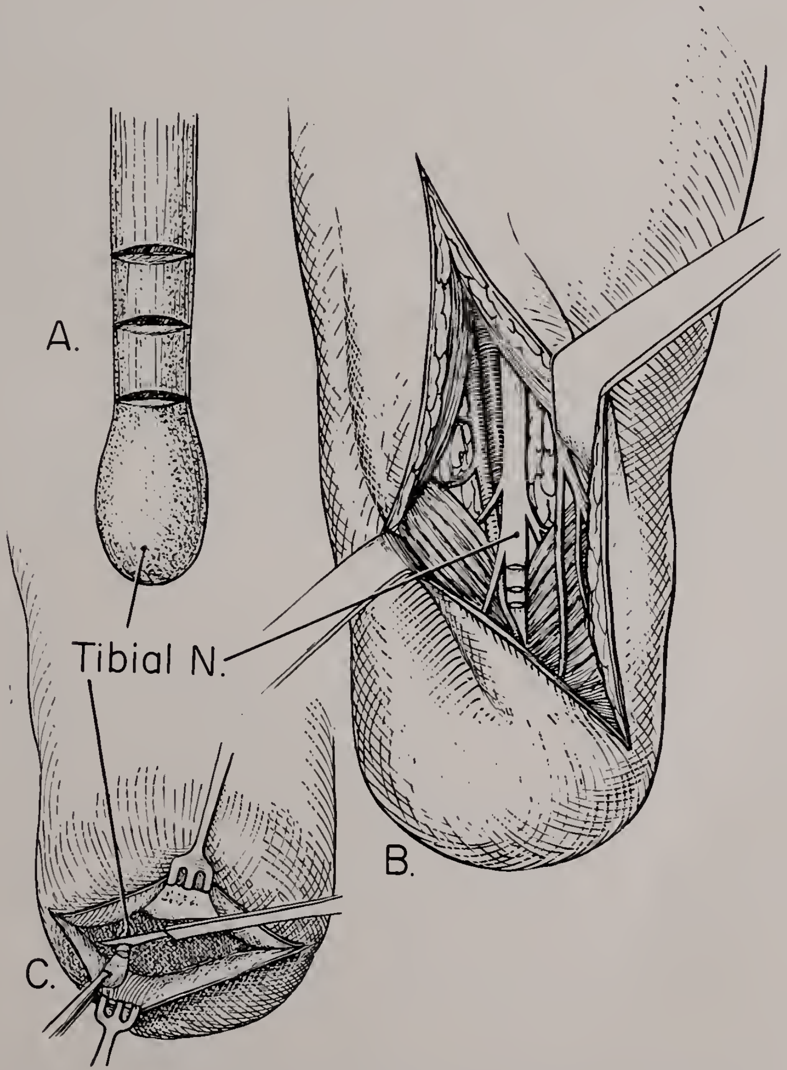

Fig. 2 — A. Proposed consecutive incisions proximal to neuroma. B. Proposed approach for B-K stump neuroma. C. Approach used in case history.

ma is presented. The patient's symptoms were completely relieved by a multiple transection and resuturing technique proposed by the late Dr. William Peyton.

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IT'S THE LAW

Humiliation and Embarrassment are Elements of Damage

A doctor should have been required to produce at the trial of a malpractice suit against him by a patient a letter written by him to his insurance carrier, in which he made a detailed statement of his handling of the patient's case, where he waived the privileged nature of the letter by sending a copy to another doctor, a Texas intermediate appellate court ruled.

The doctor testified that he left only one gauze pack in the patient's vagina after an operation and gave instructions that it was to be removed by the nurse the next day. When he visited the patient the next day, the nurse's notes indicated that the pack had been removed. The doctor made no check to determine whether it had, in fact, been removed. The patient testified that she saw the nurse remove a gauze pack the day after the operation.

A few days later, after she had left the hospital and returned to her studies at a law school, a stench developed which was extremely embarrassing since most of the school's students were male. Two weeks after the operation the patient consulted another doctor, who removed a second gauze pack from her vagina.

There was evidence from which a jury could find that the doctor negligently left a gauze pack in the patient's vagina after the operation and that the negligence was the proximate cause of humiliation and embarrassment to the patient, the court said. The patient testified that she probably would not have brought suit if the stench had been her only cause for complaint. That testimony did not make the maxim *de minimis non curat lex* (the law does not concern itself with trifles) applicable, since humiliation and embarrassment are genuine elements of damage and, under the facts of the case, could not be held insignificant as a matter of law, the court ruled.

Dobbins v. Gardner, 377 S.W.2d 665 (Tex., March 19, 1964; rehearing denied, April 16, 1964)

Between the great things that we cannot do and the small things we will not do, the danger is that we shall do nothing. — Adolph Monod

The Doctor's Visit, Jan Steen 1626-1679, Mauritshuis, The Hague

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Usual Adult Dosage: One rounded teaspoonful of Metamucil (or one packet of Instant Mix Metamucil) in a glass of cool liquid one to three times daily.

Metamucil is available as Metamucil powder in containers of 4, 8 and 16 ounces and as flavored Instant Mix Metamucil in cartons containing 16 and 30 single-dose packets.

1. Welch, C. E., Diverticula of the Alimentary Tract, in Conn, H. (editor): Current Therapy—1961, Philadelphia, W. B. Saunders Company, 1961, pp. 224-225.

SEARLE

Research in the Service of Medicine

*
She lost weight

*a result of
'METHEDRINE'® brand
METHAMPHETAMINE
HYDROCHLORIDE
therapy

Her once unruly appetite is now well tamed with 'Methedrine' (methamphetamine hydrochloride)...an easy way to help control food craving and "hunger pains."

Side effects: Insomnia may occur if taken later than 6 hours before retiring. The usual peripheral actions of sympathomimetic amines (vasoconstriction and acceleration of the heart) are minimal and little noticed on low or moderate dosage.

Complete literature available on request from Professional Services Dept. PML

Contraindications and precautions: Should not be used in patients with myocardial degeneration, coronary disease, marked hypertension, hyperthyroidism, insomnia or a sensitivity to ephedrine-like drugs. Moderate hypertension in the obese is not necessarily a contraindication since it may be relieved as the overweight is reduced.

'Methedrine' brand Methamphetamine Hydrochloride: Tablets–5 mg., scored, in bottles of 100 and 1000.

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N.Y.

Editorials

Mammography—A Screening Examination for Breast Cancer Detection?

PERFECTION OF a practical screening examination suitable for routine use in detecting early carcinoma of the breast is an eagerly sought-after goal. It is assumed that such an examination if applied on a wide scale would make earlier treatment possible for large numbers of patients and would lead to an eventual reduction in the mortality from this disease.

In the December issue* Gershon-Cohen and Pick* present a significant body of evidence supporting the use of mammography both as a routine screening examination for detection of preclinical cancer of the breast and as a means for more complete preoperative evaluation of patients with clinical breast disease. Their study demonstrates, as did a recent study from the Mayo Clinic, that in some cases carcinoma of the breast can be detected earlier by mammography than by physical examination alone. Gershon-Cohen and Pick have found 32 carcinomas in 30 patients among 1150 women given roentgenographic examinations of the breast at six-month intervals over an eight-year period. Thus 32 carcinomas have been detected in approximately 18,400 separate mammographic examinations, a detection rate of 1.7 carcinomas per 1000 examinations, closely paralleling the 1.6 carcinomas per 1000 examinations reported in the recent Mayo Clinic study.

The question then is not: Can preclinical carcinoma be detected by routine mammographic examinations done as a screening test? Rather one asks: Does the yield of carcinoma justify the effort, the expense, and the psychological impact of this examination if it is applied on a large scale? Obviously the answer depends to a great extent upon one's personal judgment. It appears to this observer that although mammography is of value in the study of high-risk patients such as those who already have had unilateral mastectomy for cancer, a yield of only 1.6 or 1.7 carcinomas per 1000 examinations is hardly adequate to justify recommendation of mammography as a routine examination in asymptomatic women. It seems that development of a practical screening examination must await either further refinement of this roentgenographic technic or the development of new technics which can detect, with accuracy, not only the earliest stages of invasive carcinoma of the breast but the in situ and premalignant stages as well.

David M. Witten, M.D.**
Rochester, Minnesota

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*Minnesota Med Vol. 47, Issue 12, Page 1449, 1964,

**Section of Roentgenology, Mayo Clinic,

**Depend on low-cost,
low-dosage Prolixin
— once-a-day**

Prolixin is a dependable tranquilizer that provides your patient with low cost therapy. No other tranquilizer costs less. Safe and convenient for office use—Prolixin in a single daily dose provides prolonged and sustained action. Markedly low in toxicity and virtually free from usual sedative effects —Prolixin is indicated for patients who must be alert. Clinical experience indicates fluphenazine hydrochloride is especially effective in controlling the symptoms of anxiety and tension complicating somatic disorders such as premenstrual tension, menopause, or hypertension—also useful for anxiety and tension due to environmental or emotional stress. When you prescribe Prolixin you offer your patient effective tranquilization that is low in cost, low in dosage and low in sedative activity.

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SIDE EFFECTS, PRECAUTIONS, CONTRAINDICATIONS: As used for anxiety and tension, side effects are unlikely. Reversible extrapyramidal reactions may develop occasionally. In higher doses for psychotic disorders, patients may experience excessive drowsiness, visual blurring, dizziness, insomnia (rare), allergic skin reactions, nausea, anorexia, salivation, edema, perspiration, dry mouth, polyuria, hypotension. Jaundice has been exceedingly rare. Photo-sensitivity has not been reported. Blood dyscrasias occur with phenothiazines; routine blood counts are recommended. If symptoms of upper respiratory infection occur, discontinue the drug and institute appropriate treatment. Do not use epinephrine for hypotension which may appear in patients on large doses undergoing surgery. Effects of atropine may be potentiated. Do not use with high doses of hypnotics or in patients with subcortical brain damage. Use cautiously in convulsive disorders.

AVAILABLE: 1 mg. tablets. Bottles of 50 and 500.

For full information, see your Squibb Product Reference or Product Brief.

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SQUIBB DIVISION Olin

Coccidioidomycosis—It Can Happen Here

Lest we fall into the error of thinking that this disease occurs only "way out there in the Southwest," attention is called to the interesting article on coccidioidomycosis in Minnesota by Strom, Hall, and Casey in the November issue of MINNESOTA MEDICINE.* It is true that the disease occurs only in those persons who have lived in or have visited the endemic areas, but this bit of travel information may not be disclosed unless the patient is questioned directly. With the increasing mobility of our population, more and more persons who live outside the endemic areas are acquiring coccidioidomycosis every year. These patients are apt to overlook the mild initial phase of the illness and later fail to associate it with eventualities when the disease again overtakes them long after their return to nonendemic regions.

A number of important factors must be kept in mind in dealing with suspected cases of fungus disease. It is not necessary for a person to remain in endemic areas for a long time in order to acquire infection with Coccidioides immitis. There is a need to suspect fungus infections in cases of obscure illness, especially of the lungs. There are few clinical findings characteristic of the fungus diseases that help to distinguish them, and pulmonary roentgenographic shadows are not specific. The diagnosis is, therefore, dependent on laboratory procedures; and except for recovery of the organism by culture, other methods leave much to be desired. The coccidioidin skin test is sometimes negative in the presence of active disease. Thus, a negative result does not rule out the possibility that the disease is present. Serologic tests are not universally available, are difficult to perform and standardize, are transitory in nature when positive, require serial examinations to be conclusive, and are subject to cross-reactions with other organisms. Sometimes, however, they are helpful and quite conclusive in making a diagnosis when cultures fail. Histologically, the infection is characterized usually by a caseous granuloma; however, this lesion is not diagnostic of coccidioidomycosis unless the organism can be positively identified in the tissue. The most reliable method of diagnosis, therefore, is culture of the organism.

Our attention has been so concentrated on the lung lesions of coccidioidomycosis that we are apt to overlook the disease in other organs, particularly the central nervous system. A history of the patient's having traveled to the endemic areas in the Southwest should always be considered important information, as it may lead to the correct diagnosis of an obscure illness.

Corrin H. Hodgson, M.D.
Rochester, Minnesota

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*Minnesota Med Vol. 47, Issue 11, Page 1189, 1964.

The Parnate-Specific Patient

The return of the antidepressant drug, Parnate (tranylcypromine — SK&F), will be welcomed by the medical profession. When Parnate was suddenly withdrawn last winter, many patients being maintained on it suffered a relapse or worsening of symptoms. Most physicians have at least a few "Parnate-specific" patients: persons who respond favorably to this compound but fail on other types of treatment. Many of these patients, after years of disability and therapeutic failure, showed striking improvement a few days after Parnate therapy was begun. Most such patients need maintenance therapy over long periods or perhaps indefi-

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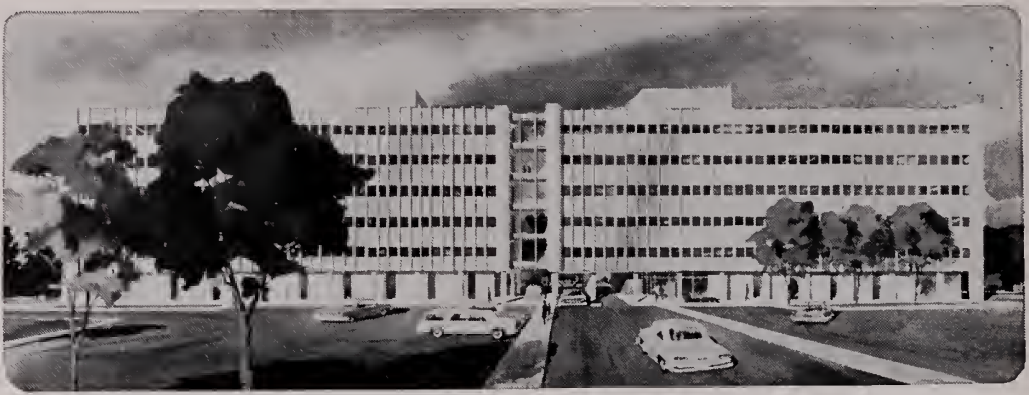

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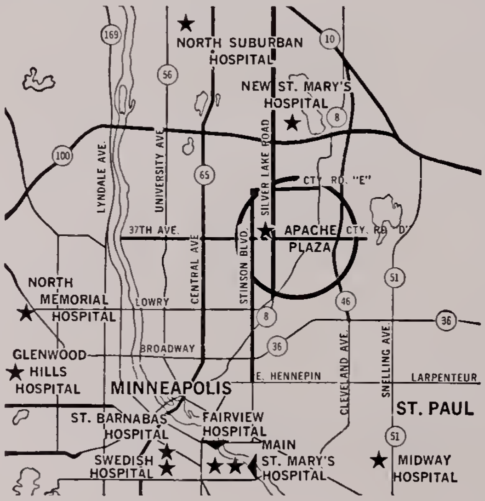
Here are some of the reasons why this will be the ideal location for your new office:


169
NORTH SUBURBAN HOSPITAL
10
56
NEW ST. MARY'S HOSPITAL
8
100
LYNDALE AVE
UNIVERSITY AVE
65
SILVER LAKE ROAD
CTY. RD. "E"
37TH AVE.
CENTRAL AVE
STINSON BLVD.
APACHE PLAZA
CTY. RD. "D"
51
46
NORTH MEMORIAL HOSPITAL
LOWRY
8
36
BROADWAY
36
GLENWOOD HILLS HOSPITAL
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- Ample free parking for everyone, reserved parking for doctors.
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- Handy to Twin Cities hospitals.
- Attractive, dignified building, giving you the best professional address north of either loop.
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nitely if they are to retain their improvement. Clear-cut Parnate responders are not common, but they do occur in significant numbers. For example, in a recent survey, 55 Minnesota psychiatrists recalled 603 such Parnate-specific cases during the three years when the drug was available. The occurrence of these definite and often dramatic therapeutic results has been one of the chief factors accounting for the intense interest shown in this compound. Letters by hundreds of physicians from all parts of the country appear to have been a factor in leading the FDA to conclude that the drug was not expendable and that its benefits were worth the risk.

Parnate will be re-introduced with revised prescribing directions which contain a refreshing comment regarding the high incidence of placebo response and spontaneous improvement in depressed patients. The new labeling, in addition, contains a number of restrictions and precautions which, if followed, should lessen the frequency and severity of adverse reactions. Also, the fact that the drug was withdrawn from the market and the publicity subsequent to this should make physician and patient alike aware of the hazards involved.

A major difficulty encountered, even with the new labeling, concerns the definition of that patient most likely to respond favorably to Parnate. Listing "severe mental depression" as the chief indication for Parnate, the revised prescribing directions go on to state that Parnate may aggravate co-existing agitation and anxiety. In actual practice, however, many types of patients respond to this agent. While usually an element of depression or withdrawal may be found, Parnate-specific cases occur among some schizophrenics, especially catatonics, some chronic neurotic patients with anxiety, and mildly-depressed but fearful and anxious patients. Many of these, however, would not fit in under the heading of "severe depression," as recommended in the revised prescribing directions.

Admittedly, the identification of the potential Parnate-responder is a difficult task, as reliable predicters are lacking for all psychotropic drugs. Physicians may get some help from the formal diagnosis and from target symptoms, but all too often they must fall back on trial and error. We suspect that there is some type of biochemical or physiological difference between those who respond to MAO inhibitors, such as Parnate, and those who do not. Since clinical symptoms do not differentiate these two groups, we badly need a test, possibly a physiological one, which would have predictive value. Let us hope that research will soon provide the answer.

Burtrum C. Schiele, M.D.
Smith Kline & French Laboratories

Diet and Cholesterol

Two SCHOOLS of thought, if not more, are apparent in most areas of medicine. The one under consideration has led to an excellent cartoon with the caption, "Are you a cholesterol-is-all doctor or a cholesterol-is-all-nonsense doctor?" As time goes on and more data become available, evidence is favoring an intermediate position — as is often the case. Data from the large, long-term, prospective epidemiologic study in Framingham have indicated, with little doubt, that there is a direct relationship between the level of blood cholesterol and the incidence of coronary heart disease in men aged 30 to 59 years and women aged 40 to 49 years. Furthermore, as might be anticipated from experience in other areas of medicine, there is no sharp cut-off point or "normal limit," but rather an increase in incidence of coronary heart disease with increasing levels of cholesterol from less than 200 mg. per 100 ml. to those in excess of 260 mg. per 100 ml. The morbidity ratio from coronary heart disease in men aged 30 to 49 years in the latter group is

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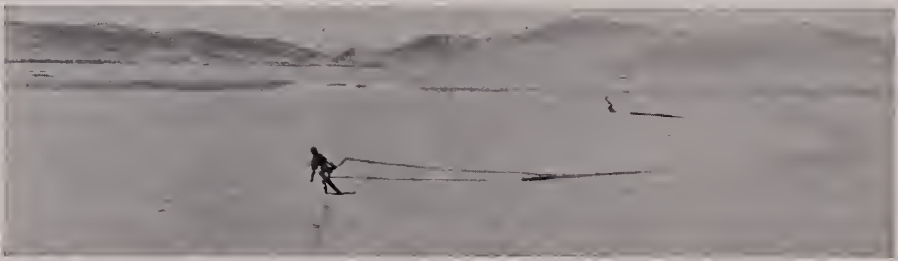
ONE WAY TO TRY TO
AVOID COLDS AND
SINUSITIS IS TO
GET AWAY FROM
FRIGID WEATHER



...but if your patient can't get away, relieve sneezing, running nose, and congestion of colds and sinusitis all day or all night with one

ORNADE® Trademark **SPANSULE®** brand of sustained release capsules

Each capsule contains 8 mg. of Teldrin® (brand of chlorpheniramine maleate), 50 mg. of phenylpropanolamine hydrochloride, and 2.5 mg. of isopropamide, as the iodide.

Summary of contraindications, cautions and side effects: Do not use in patients with glaucoma, prostatic hypertrophy, stenosing peptic ulcer, pyloric duodenal obstruction, or bladder neck obstruction. Use with caution in the presence of hypertension, hyperthyroidism, or coronary artery-disease. Drowsiness; excessive dryness of nose, throat or mouth; nervousness or insomnia may occur on rare occasions but are usually mild and transitory.

Before prescribing, see SK&F Product Prescribing Information.

Smith Kline & French Laboratories SK&F

more than fivefold that in the former. The factors influencing the level of blood cholesterol, although not all clearly understood, do include hereditary as well as dietary factors. Unfortunately, there is still no evidence to establish firmly that lowering the level of blood cholesterol by any means presently available will prevent, arrest, or reverse coronary or peripheral atherosclerosis.

Despite these shortcomings, continued careful research on the causation and control of elevated levels of blood cholesterol in humans is needed.

The interesting observations made by Dr. Herbert W. Johnson during medical mission service in Tanganyika, reported in the November issue of MINNESOTA MEDICINE,* suggest a relationship between saturated fat in the diet and the level of blood cholesterol in an ethnic subgroup not previously studied. Although the relatively small number of samples and the wide range of values for cholesterol do not permit firm conclusions, the data presented do add support to the concept that the dietary intake of saturated fat is an important factor as it relates to the level of cholesterol in the blood. Research currently in progress may answer the all-important question: Will a decrease in the dietary intake of saturated fat have a beneficial effect on the incidence of coronary heart disease?

Kenneth G. Berge, M.D.
Rochester, Minnesota

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*See Minnesota Med Vol. 47, Issue 11, Page 1413, 1964.

Test Your Word Score

The Editors have picked difficult words from the manuscripts contained in this issue and list them below with their definitions. Test Your Word Score! If you know all nine words and their meaning, you have superior intelligence. If you find you know only six, you still have excellent intelligence; five, good, and four, fair. However, a score of three and below, rates only a "poor."

Watch for the asterisks in the manuscripts each month and test your word sense!

For your Word Score:

Donovanosis — granuloma inguinale (see page 309)

de novo — anew, afresh (see page 310)

hamartomas — a focal malformation resembling a neoplasma (see page 311)

cor triatriatum — heart with three atrial chambers (see page 324)

causalgia — a burning pain (see page 348)

hypalgesia — diminished sensation (see page 371)

dysmetria — improper measuring of distance in muscular acts (see page 376)

His job is too big for his wife's breeches. — C.O.R.

Should money earned on investments by doctors and dentists be tax free?

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If you are in a high income bracket your investment profits may amount to 1% **after Federal and State taxes.** Tax-free bonds give you a greater yield that you can keep! Find out what taxable investments really earn, **after taxes,** based on **your** income bracket . . . and find out how these earnings compare with tax-free bonds.

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The Editor's Soliloquy

Mob Psychology

In adopting Medicare, are we not capitulating to mob psychology in our eagerness to find a solution for a few minor ills: crashing through a jungle instead of charting a course? The voice of mob psychology is not the aggregate of individual voices; it is an irrational, ephemeral, pernicious phenomenon which might for the moment seem to constitute consensus, but is nevertheless no valid index of social enlightenment or progress. This voice can define conservatism as extremism and can promulgate a casual off-the-cuff remark as documentary evidence. It can compel us to adopt laws, practices, ventures, attitudes that in our saner moments we would never have considered, which may require years to transcend. It can produce an evil image, unjustified and unjustifiable, which cannot be erased.

It is safe to say that the American Medical Association and all physicians are eager to provide hospital and medical service to and for all people; but we cannot envision lasting benefits from a plan that has been devolved from the hysteria of mass neurosis and political expediency.

Carl O. Rice, M.D.

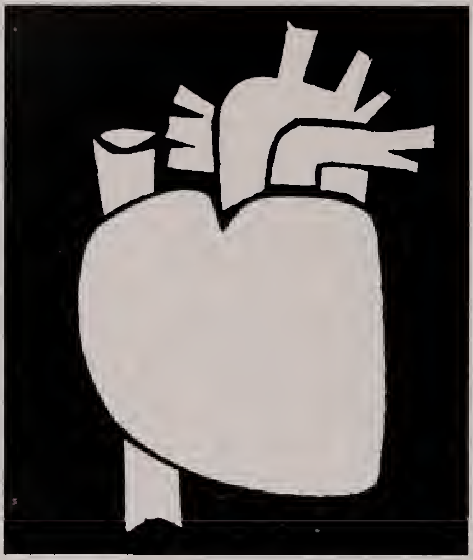
President's Letter Continued from Page 307.

American Medical Association supports the fullest implementation of the Kerr-Mills Bill enacted into law in 1960. This law revised existing provisions for federal participation in old-age assistance programs and established a new federal grant-in-aid to assist states in the payment of health services for those more than 65 years old who require financial aid only for health care. Complete and unlimited care is possible through this mechanism. The law permits the individual states wide latitude in creating a program to meet the needs of their medically indigent. The American Medical Association has recommended that eligibility for such care be simply and easily determined, outside the mechanism of the welfare services, and that administration be carried out under some other department of the government than the welfare department. Physicians in Minnesota should inform themselves about the provisions of the Kerr-Mills Law and Minnesota Medical Assistance for the Aged, so that they can answer questions raised by their patients or the public.

In subsequent letters I shall discuss the actions taken by the House of Delegates of the American Medical Association at the special session of the delegates, and some of the plans which have been suggested by groups of physicians in Minnesota and elsewhere.

"Let us therefore brace ourselves to our duties and so bear ourselves that, if the British Empire and its commonwealth last for a thousand years, men will say: "This was their finest hour." — Winston S. Churchill — Speech in the House of Commons, June 18, 1940 — the day of the French capitulation.

A CONSERVATIVE Rx
FOR A CLASSIC Dx



SUDDEN ONSET
ANTERIOR
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MILTRATE®

meprobamate 200 mg. + pentaerythritol tetranitrate 10 mg.

Long-acting coronary vasodilation plus effective tranquilization for prophylaxis of pain in angina pectoris

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Indications: 'Miltrate' is useful for prophylaxis of pain in angina pectoris, especially where accompanied or intensified by anxiety. **Contraindications:** Like all nitrates, pentaerythritol tetranitrate should be avoided or prescribed cautiously for patients with glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use. **Precautions:** *Meprobamate* —Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies. **Side effects:** Side effects of 'Miltrate' administration have been few, consisting of headache, nausea, sleepiness and insomnia, and dizziness. *Pentaerythritol tetranitrate*—The most common side effects are transient headache, nausea, and rash. Weakness, palpitation, flushing, gastrointestinal distress, and lightheadedness have been reported on a few occasions. *Meprobamate*—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse. **Dosage:** Usual dosage is one or two tablets before meals and at bedtime. Individualization of dosage is required for maximum therapeutic effect. Doses above 12 tablets daily are not recommended. (Note: When titration of the doses of the individual components of 'Miltrate' is desired, meprobamate is available as 'Miltown' [meprobamate] tablets and 'Meprospan' [meprobamate, sustained release] capsules.) **Supplied:** White tablets, each containing meprobamate 200 mg. and pentaerythritol tetranitrate 10 mg. ***Before prescribing, consult package circular.***

WALLACE LABORATORIES / Cranbury, N. J.

CML-5116

Curbstone Consultation

Cystinuria

QUESTION: I would like to know something concerning future management for a patient of mine with a diagnosis of cystinuria and recurrent cystine stone formation. What measures can I employ, if any, to discourage the formation of these stones?

ANSWER: Cystinuria represents an inborn error of metabolism. In this disease there is increased excretion of the amino acids, cystine, arginine, ornithine and lysine. In the kidney each competes against the others for a common tubular reabsorptive mechanism. Though excretion of one of the other amino acids may exceed that of cystine, the cystine stones form because of their limited solubility. Although the cystine stones are more insoluble in acid then alkaline urine, alkalinizing the urine is generally not utilized in the programs of management for these patients because of the rather small increase in solubility of such stones that follow even large increases in the pH of the urine. Principal management, therefore, centers around maintaining large urinary outputs to provide a volume sufficient to hold the cystine in solution. The efficacy of restricting foods in the diet rich in methionine and cysteine (which are converted to cystine) is not well established.

Myocarditis and Measles

QUESTION: How frequently is myocarditis encountered as a complication of measles? Is the pathogenesis of the myocardial changes due to a direct invasion of the myocardium by the virus?

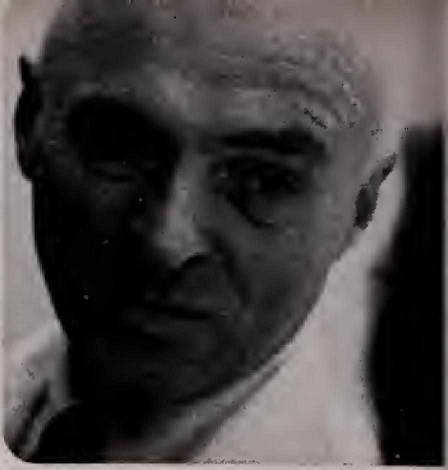
ANSWER: Measles myocarditis is a rarely reported complication. However, among fetal cases of measles it may be found at autopsy in up to four per cent of the cases. In one study concerned with a determination of the incidence of measles myocarditis among cases of myocarditis in acute infectious diseases in children, about two per cent resulted from measles, and in all such cases the complication of severe bronchopneumonia existed.

In this condition direct invasion of the myocardium by the virus has been incriminated, as well as vasculitis, tissue anoxia, and circulating toxins. It presently remains in doubt as to which view is correct.

Don't hesitate to be as revolutionary as science. Don't hesitate to be as reactionary as the multiplication table. — Calvin Coolidge

Buy you a cup of coffee?

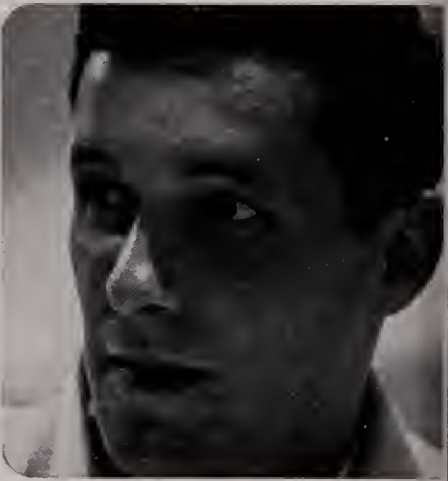
Fine! This last patient...



Mrs. Jones?

Yes, sir. She's down to 140/85.

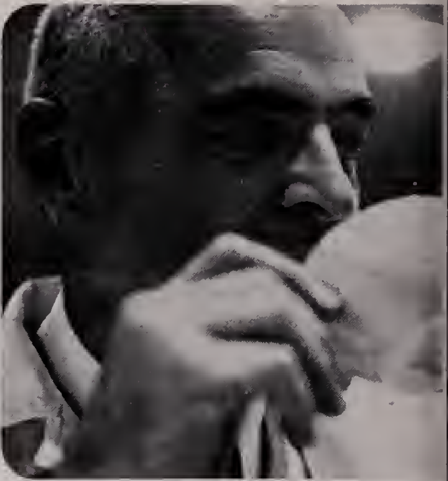
Right. When we started, she was 195/120.



Is that Regroton again?

I use it for all my hypertensives.

Does Regroton always work this well?



Not always. But the exception prove the rule.

Composition: Each tablet contains chlorthalidone, 50 mg., and reserpine, 0.25 mg.
Contraindications: History of mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.
Warning: Discontinue 2 weeks before general anesthesia, 1 week before electroshock therapy, and if depression or peptic ulcer occurs.
Precautions: Reduce dosage of concomitant antihypertensive agents by one-half. Discontinue if the BUN rises or liver dysfunction is aggravated. Electrolyte imbalance and potassium depletion may occur; take particular care in cirrhosis or severe ischemic heart disease, and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended. Use with caution in patients with ulcerative colitis, gallstones, or bronchial asthma.
Side Effects: Nausea, vomiting, diarrhea, muscle cramps, headaches and dizziness. Potential side effects include angina pectoris, anxiety, depression, drowsiness, hyperglycemia, hyperuricemia, lassitude, leukopenia, nasal stuffiness, nightmare, purpura, urticaria, and weakness.
For full details, see the complete prescribing information.

Availability: Bottles of 100 and 1000 tablets.
Average Dosage: One tablet daily with breakfast.

*Chupkovich, V.; Finnerty, F. A., Jr., and Kakaviatos, N.: The value of chlorthalidone plus reserpine in moderately severe and severe hyper tension: A two year study. Presented at the 7th Inter-American Congress of Cardiology, Montrea June 14–19, 1964.

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Regroton® outperformed other antihypertensives in 95% of patients*

Geigy

Fracture–Trauma Conference

The Limping Young Teenager

Slipped Upper Femoral Epiphysis

Early diagnosis of slipped upper femoral epiphysis may result in treatment preventing permanent disability of the hip.

The entity is primarily an idiopathic disorder of the epiphyseal line of the femur adjacent to the head. As a result of a widened, softened, and weakened line, the head displaces posteriorly and in varus from its usual relationship with the neck of the femur.

Acute Slip

Most dramatic is the acute, total displacement traumatically without antecedent symptoms. This individual is between twelve and sixteen. His examination is similar to the older individual with fractured neck of the femur with displacement. Recognition of hip disorder is easy and X ray confirms the diagnosis (Fig. 1). Urgent reduction and internal fixation are indicated. Some cases will eventuate in arthrosis secondary to vascular loss. Delay in treatment increases incidence of avascular necrosis of the head.

Chronic Slip

Onset is so subtle that the individual cannot accurately recall the duration. More deceiving are the symptoms. They do not lead the patient or examiner to the hip in a large number of cases. Distress appears centered on the thigh or toward the knee. A limp may be noted by the teenager's friends or parents long before the patient has admitted symptoms. Frequently, the limp and distress may disappear for a few weeks at a time. Disability is increased in subsequent attacks.

In the full syndrome, the patient may have some distress in the groin. Characteristically, he walks with a limp, the hip and knee flexed. The whole extremity is in external rotation from the hip. Passive motion of the hip may be one-half or one-third of normal. Greatest loss is of internal rotation. There is atrophy of the thigh musculature. Didactically, the patient has been described as the Froelich-type fat boy, but slip can occur in any body build prior to fusion of the epiphyseal line.

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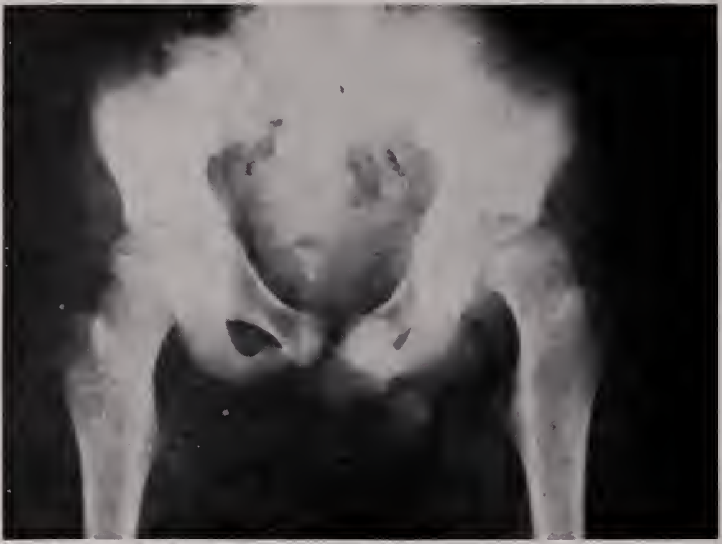

Fig. 1 — Acute slipped upper femoral epiphysis, left.

X ray in the Chronic Slip

There is slow progression from normal position of the head to gross displacement. All individuals suspected of hip trouble should have two views of the hips. The first is an anteroposterior view of the pelvis, the common view, and the most frequently misinterpreted. Widening and irregularity of the epiphyseal line unilaterally are noted. The head may not have shifted enough to alter the normal head and neck relationship.

Diagnostic from the beginning are lateral X rays of the hips taken with the legs in the frog-leg position (Fig. 2). The widened epiphyseal line may be seen, but slipping of the head posteriorly is readily determined (Fig. 3).

Progression of symptoms is associated with further slipping, with varus easily recognizable on the anteroposterior view of the pelvis. A lateral X ray will show posterior angulation of the axis of the head on the axis of the neck up to 60° or 70°. The bone of the superior portion of the neck tends to round off. The inferior neck seems to thicken and drift along with the displacing head.

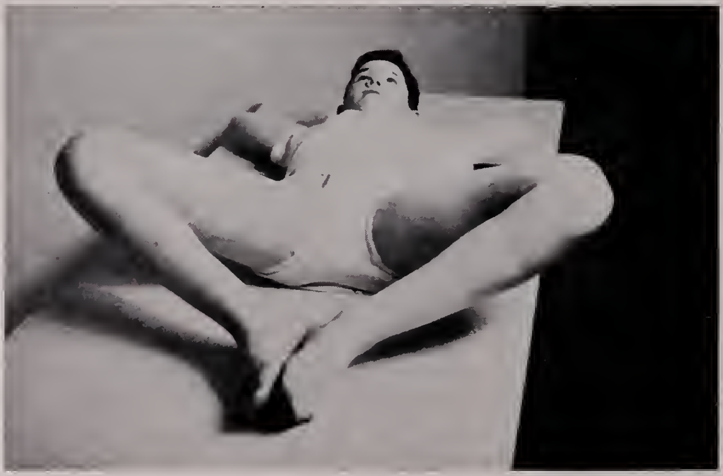

Fig. 2 — Position for frog-leg X ray of pelvis.

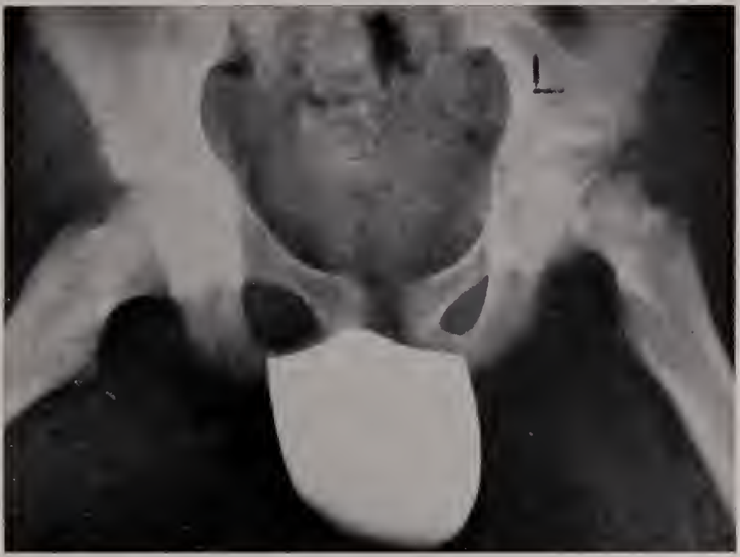

Fig. 3. — Chronic slipped upper femoral epiphysis, left.

Treatment in the Chronic Slip

Urgent care is recommended in all cases hoping to prevent the complete slip and its serious consequences. In-situ fixation with pins, screws, or threaded wires is performed in those cases having less than thirty degrees change in the axis of the head and neck. This may be expressed as the head being off less than one-third of its diameter. The outlook in these cases is good. Full weight-bearing is permitted in three months.

Guarded prognosis is given when the head is displaced more than thirty degrees or more than one-third of its diameter. In-situ nailing may lead to early arthrosis because of malalignment of the head and acetabulum and the loss of normal internal rotation of the hip.

When the line is wide and appears nonossified, gentle but firm manipulation on the fracture table preoperatively may reduce the displacement to a degree where pin fixation in the new position is indicated (Fig. 4). One can expect a percentage of these cases to have avascular necrosis of the head, but this percentage should be smaller than in cases having open cervical osteotomy.

The major slip may be treated by open replacement after osteotomy through the epiphyseal line. Upward to forty percent of these cases have vascular changes in the head leading to arthrosis.

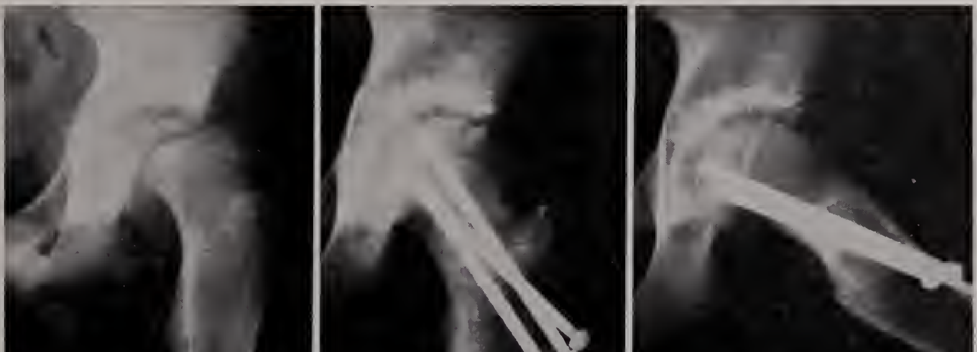

Fig. 4 — Method of internal fixation by Knowles' pins.

Continued

Certain cases with severe slip have been treated by in-situ nailing of the head, and internal rotation osteotomy of the upper femoral intertrochanteric area. This remote osteotomy is an attempt to avoid avascular necrosis.

Treatment in Late Cases (Epiphyseal Line Closed)

This is the only group in which surgery is not urgent. Treatment is directed toward reduction or prevention of arthrosis. Cervical or trochanteric osteotomy may be indicated. Spontaneous ankylosis in untreated cases, or arthrosis following surgery may be treated by cup arthroplasty or, more rarely, prosthetic replacement.

This Series 1953 to 1963

Seventeen individuals comprise this series. Their ages at the time of operation were between 10 and 16 years. Five cases had acute total slips of the epiphysis treated by immediate operation and fixation with Knowles pins. In this group, one patient had a moderate necrosis with no change in the joint line. This individual may develop an early osteoarthritis. The other case of necrosis was associated with some hypertrophic lipping at the junction of the slipped epiphysis. There was minimal limitation of motion in this hip. Thus, two out of five hips were complicated by avascular necrosis.

Fourteen hips were involved with a slow slip. Five of these were nailed in situ without manipulation. Four in-situ nailings resulted in excellent function clinically and by X ray. One in-situ nailing was more than one-third off but shows a good result. Five slow-slipping epiphyses were treated by manipulation, improvement in position, and fixation with Knowles pins. So far no necrosis has been noted in these ten cases of slow slip.

In one severe slow slip, cervical osteotomy was done with good functional result but obvious necrosis of the head with alteration of the femoral head and neck.

Two individuals with more than one-third slip were treated by in-situ fixation of the femoral head and neck and subtrochanteric osteotomy held by Jewett nails. The osteotomy was to correct varus and external rotation deformity.

One bilateral case was recognized only five years after acute slip when checked on an Army examination. The untreated hip had slipped considerably into varus and posteriorly, but the patient insisted that he had never had symptoms. This followed an original total slip on the right which had been fixed by Knowles pins. At that time the hip X rays were normal on the left side. The patient was emphatic about total absence of symptoms in the left hip, though it had slipped about 40 to 50 per cent.

Bilateral cases were 17.5 per cent or the reported average. Only two cases of the 17 were girls.

Conclusion

Early recognition of slipped upper femoral epiphysis may be expected through suspicion, examination, and especially frog-leg lateral hip X rays. Early treatment by in-situ internal fixation in a slip of less than one-third can lead to excellent lifelong results. Prognosis after slip of more than one-third the diameter of the head must be guarded no matter how skillfully surgery is executed. Delay, traction, or casts are to be avoided because the displacement can increase or become complete, thereby leading to poor results. Arthrosis and even ankylosis may result in untreated cases. As the other hip may become involved, the physician, patient, and family should be alert to any complaint. The individual is not free from hazard until the epiphyseal line is closed.

A busy practitioner may see only one or two cases in a lifetime. Early recognition and treatment can prevent a crippling hip disorder.

Kenath Sponsel, M.D.
Minneapolis, Minnesota

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Oral Surgery on President Cleveland in 1893

(As Narrated by W. W. Keen)

Doctor Hasbrouck first extracted the two left upper bicuspid teeth (very badly ulcerated) under nitrous oxide. Doctor Bryant then made the necessary incisions in the roof of the mouth, also under nitrous oxide.

At one-fourteen P.M. ether was given by Doctor O'Reilly. During the entire operation Doctor Janeway kept close watch upon the pulse and general condition. Doctor Bryant performed the operation, assisted by myself and Doctor Erdmann.

The entire left upper jaw was removed from the first bicuspid tooth to just beyond the last molar, and nearly up to the middle line. The floor of the orbit — the cavity containing the eyeball — was not removed, as it had not been attacked. A small portion of the soft palate was removed. This extensive operation was decided upon because we found that the antrum — the large hollow cavity in the upper jaw — was partly filled by a gelatinous mass, evidently a sarcoma. This diagnosis was later confirmed by Dr. William H. Welch, of the Johns Hopkins Hospital, who had also examined the former specimens.

The entire operation was done within the mouth, without any external incision, by means of a cheek retractor, the most useful instrument I have ever seen for such an operation, which I had brought back with me from Paris in 1866. The retention of the floor of the orbit prevented any displacement of the eyeball. This normal appearance of the eye, the normal voice, and especially the absence of any external scar, greatly aided in keeping the operation an entire secret.

Only one blood vessel was tied. Pressure, hot water, and at one point the galvanocautery, checked the bleeding. The hemorrhage was not large, probably about six ounces — say, a tumblerful — in all. At the close of the operation, at one-fifty P.M., the pulse was only eighty. The large cavity was packed with gauze to arrest the subsequent moderate oozing of blood. At two-fifty-five P.M. a hypodermic of one-sixth of a grain of morphine was given — the only narcotic administered at any time.

What a sigh of intense relief we surgeons breathed when the patient was once more safe in bed can hardly be imagined![*]

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[*] Rapport, Samuel, and Wright, Helen: Great Adventures in Medicine. The Dial Press, New York, 1952, p. 477-478.

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Niacinamide	100 mg.
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Tumor Conference

Retroperitoneal Fibrosis Simulating Carcinoma of the Pancreas

Report of A Surgically Treated Case Complicated by Fatal Postoperative Hemorrhage

Retroperitoneal fibrosis is itself an uncommon disease and documented involvement of the pancreas by this process is extremely rare. The following case is presented because of the unusual manifestations of the disease and because of a fatal complication from the operation utilized to treat it.

Case Report

A 73-year-old white male was admitted to Ancker Hospital on September 30, 1963, with a history of progressive numbness and weakness of his extremities for over a year. In 1954 a posterior fossa astrocytoma had been removed.

Physical Findings

Pertinent physical findings at time of admission were confined to the nervous system and included marked loss of deep sensation and moderate peripheral and distal muscle weakness, greater on the right than on the left. Moderate hypesthesia and hypalgesia,* most marked on the right leg, truncal ataxia and mild bilateral cerebellar signs were present. There was no jaundice, dark urine or light stools.

Laboratory Findings

Laboratory findings included a hemoglobin of 12.6 gm. per 100 ml., a white blood count of 8,550 per cu. mm. with a normal differential, and a normal urinalysis. Lumbar puncture: cerebrospinal-fluid pressure-180 mm. water, 20 lymphocytes/cu. mm., sugar 65 mg.% and protein 58 mgm.%. Skull roentgenograms showed no change in the appearance of postoperative defects noted on previous roentgenograms or in the position of metal clips. Diagnoses of recurrent cerebellar tumor or peripheral neuropathy were considered. There was no definite evidence to support the former diagnosis. A radioactive brain scan was negative. As part of the investigation an upper gastrointestinal roentgenographic study demonstrated a persistent narrowing in the region of the gastric antrum. Gastroscopy disclosed what appeared to be a fungating mucosal lesion in the distal portion of the stomach.

Findings at Operation

At laparotomy on December 16, 1963, a stony hard mass measuring 4 cm. in greatest dimension was seen evolving from the head of the pancreas to deform the antrum. This mass was adherent to surrounding structures including the inferior vena cava. The

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*See Test Your Word Score Page 359.

Continued

common bile duct was moderately dilated. Although the mass simulated a carcinoma of the head of the pancreas, multiple biopsies from the periphery of the mass submitted for frozen sectioning were reported as being comprised of dense fibrous tissue negative for carcinoma. Because the organ appeared grossly involved by a malignancy, a pancreatoduodenal resection was carried out. The pancreas was anastomosed to the jejunum by invagination of the cut end into the open end of the jejunum. An end-to-side choledochojejunostomy and posterior gastrojejunostomy completed the repair.

Pathologic Findings

Histology of the mass in the head of the pancreas showed no neoplasia. Instead, there was dense fibrosis with an occasional focal aggregate of lymphocytes and a few scattered ones (Figure 1). Also, a few variable-sized nerve trunks were encompassed by the fibrous mass. The tissue diagnosis was that of a localized mass of pancreatic fibrosis with evidence of minimal chronic inflammation.

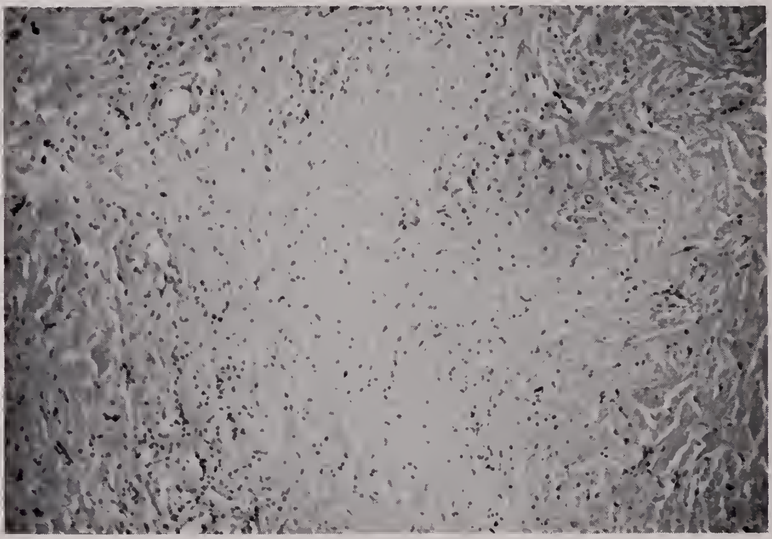

Fig. 1 — Photomicrograph showing dense collagenous fibrous tissue and scattered lymphocytes. (Hematoxylin and eosin x 100).

Postoperative Course

The patient's postoperative course was uneventful until two days postoperatively when the abdominal incision began to drain a small amount of serosanguinous fluid. The wound was explored under local anesthesia and disclosed a broken figure of eight-wire suture in the fascial closure. This was replaced. Following this the patient gradually improved and progressed in a satisfactory manner until December 27, 1963, when an anemia of 9.1 gm.% hemoglobin was noted. Two units of whole blood were given. On January 14, 1964, the patient developed massive gastrointestinal bleeding which failed to respond to transfusion and nonoperative measures. At operation a gastrotomy demonstrated profuse bleeding originating in the proximal loop. This loop was opened in the region of the pancreatojejunal anastomosis, and the bleeding was seen to originate in a large ulcerated area in the end of the pancreas at the point where this organ had been invaginated into the jejunum. The bleeding was controlled with considerable difficulty by oversewing the ulcerated area. The patient's postoperative condition was unsatisfactory and he died a few hours later.

At autopsy the pancreatojejunal anastomosis showed digestion of pancreatic substance and small bowel mucosa as well. A branch of the splenic artery had projected into the ulcerated area and had been tied with a silk suture. Splenic infarction had occurred secondary to inadvertent ligation of the splenic vein by another suture which had been placed in an attempt to control the bleeding. The inferior vena cava was surrounded but not invaded by a fibrous mass which had a similar appearance to that of the mass in the previously excised segment of pancreas. There was no evidence of classical retroperitoneal fibrosis in the region of sacrum. The ureters were of normal calibre and free of obstruction. There was nothing to suggest a sclerosing cholangitis. The brain showed dilated lateral ventricles, more marked on the left, and prominent narrowing of the white matter of the cerebral hemispheres, again more marked on the left. There was also slight dilatation of the third ventricle. An additional finding was that of a small hemorrhage into the base of the left side of the pons. The cerebellar hemispheres were free of recurrent tumor.

Discussion

Although Albarron is credited with the first description of retroperitoneal fibrosis in 1905,[1] Ormond's[2] report in 1948 of two patients with involvement of the ureters established this condition as a clinical entity. This latter study was the stimulus for the subsequent recognition and reporting on many patients. Most of these reports have appeared in the urological literature, because ureteral obstruction by the fibrous mass has been the common manifestation of the disease.

Involvement of the biliary tract and pancreas by retroperitoneal fibrosis is a less frequent manifestation. Whether primary sclerosing cholangitis is the same disease or a variation of it has not been settled. Schwartz and Dale[3] reviewed 13 cases of primary sclerosing cholangitis and added six of their own. In some patients the entire area of the extrahepatic biliary tree was encompassed in dense adhesions. Usually, however, there was diffuse thickening of the walls of the extrahepatic biliary tract with encroachment upon the lumen. The duct system was completely involved or the hepatic ducts spared and the disease restricted to the length of the common duct. Bartholomew and associates[4] have documented the apparent progression of sclerosing cholangitis to typical retroperitoneal fibrosis in one patient.

We have been able to find only one other patient with involvement of the pancreas by retroperitoneal fibrosis where this lesion was grossly indistinguishable from carcinoma of the pancreas.[4] Cameron and associates,[5] Raper,[6] and Schneider,[7] have described patients with retroperitoneal fibrosis, whose pancreas as well as other retroperitoneal structures were involved in the diffuse fibrous mass.

The fatal bleeding which occurred in this case would appear to be a complication of the end-to-end pancreatojejunostomy[8] rather than of the disease. At the Mayo Clinic Monge and associates[9] discussed their experience with 65 patients who had undergone pancreatoduodenal resection from carcinoma of the periampullary region from 1949 through 1955 and discovered that the most common method of reconstruction was end-to-end pancreatojejunostomy with end-to-side choledochojejunostomy and distal polya gastrojejunostomy. Four of their five patients with postoperative gastrointestinal bleeding died. These authors caution that the greatest postoperative danger is from autodigestion of tissues near the pancreatojejunal stoma with resultant bleeding. This complication accounted for half of the surgical deaths in their series. Massive bleeding in the case report described herein was the result of digestion and ulceration of pancreatic substance exposed in the jejunal lumen at the end-to-end pancreatojejunal anastomosis. This is an intrinsic defect in this type of union of the pancreas to the small intestine and, in the authors' opinion, contraindicates its use. It is apparent that once the complication of bleeding from

Continued

this site developed, only total removal of the remaining pancreas could permanently control the bleeding. Unfortunately this was not done. End-to-side pancreatojejunostomy with careful approximation of pancreatic duct to jejunal mucosa and buttressing of the end of the pancreas with the serosa of the jejunum is a much safer anastomosis. If the pancreatic duct is small, the anastomosis can be made over a stent which will pass into the intestine in a few days.

Summary

A patient with retroperitoneal fibrosis grossly indistinguishable from carcinoma of the pancreas, who was treated by radical pancreatoduodenectomy, is described. Postoperative bleeding resulted from erosion of the pancreas exposed in the jejunal lumen. In light of this complication this type of anastomosis should not be utilized for reconstruction following pancreatoduodenal resection.

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James W. LaFave, M.D.*
William B. Carpenter, M.D.*
St. Paul, Minnesota

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*From Departments of Surgery and Pathology, Ancker Hospital, St. Paul, Minnesota and University of Minnesota Medical School, Minneapolis, Minnesota.

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Are you a thoroughbred? It has been well said that the cart horse goes until he can't go another inch and then gives up; that the thoroughbred goes until he can't go another inch — and then goes the other inch. — Forbes Epigrams

Fortunately the future only comes one day at a time. — Herbert Prochnow

Unavoidably yours. — Leo Rosten

Neuro-Pediatrics Conference

Mental Retardation and Hearing Loss*

A six-and-one-half-year-old white female was referred to the University of Minnesota Hospitals on August 18, 1964, for evaluation of speech abnormality and possible mental retardation. The child had been treated several times for recurrent upper respiratory infections and otitis media. She is a mouth-breather, and the question of hearing-speech defect was raised by the parents. Neither mental nor emotional problems are apparent within the family. Because of the disturbing influence upon the family of pressure from neighbors and due to parental concern, Dr. Wm. Rice** recommended speech and hearing evaluation. He feels that the mother has been the most noticeable of the patient's problems; however, he feels she is quite mature and understanding of the situation.

Mr. Martin Kammermeier***

Examination in February, 1963, revealed that the child's speech was almost unintelligible, and because of her short attention span and hyperactivity, it was impossible to administer formal tests of articulation. Hearing tests were not given because of her extreme hyperactivity. She was able to repeat most sounds correctly, and examination results of her speech mechanisms were normal. She was observed to be a mouth-breather and to have a "chronic mild cold."

Psychological testing at St. Cloud State Teachers' College revealed an I.Q. of 77 on a Stanford-Binet test. Trial speech therapy under an advanced therapist was given from July 17 through August 17, 1963. There was no improvement in her speech, and the only progress made was that "she did not whisper as much."

Dr. James Zeese†

The child is a product of a full-term pregnancy and normal delivery. Her growth and development have been normal except that she did not walk until eighteen months. Toilet training was accomplished at two years of age and presented no difficulties. Her early speech development appeared

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*Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatric conferences are held the first and third Wednesdays of every month from 3:15 to 4:15 p.m. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Robert W. ten Bensel, in Pediatrics, and Dr. Robert Soll, in Adult Neurology.

**St. Cloud physician.

***St. Cloud State College Speech and Hearing Service, St. Cloud, Minnesota.

†Senior Medical Student.

Continued

normal; as an infant she babbled, cooed and generally vocalized like any other child. She used single words at two years, and a combination of words shortly thereafter. It was not until the child was four years old that the mother became aware that her little girl was not as intelligible as other children. At this age, she would satisfy her wants by a minimum of vocalization accompanied by appropriate gestures.

At age five the child had measles with no sequelae. The father states that she is very clumsy and unco-ordinated, with a short attention span. There is no history of convulsion, head trauma, or other neurological symptoms.

Family history shows that the parents are both living and in good health, as well as three siblings. One of the mother's first cousins died of muscular dystrophy in the teens, and another is mentally retarded, presumably from birth injury.

Physical examination showed a hyperactive six-year-old female with a short attention span. At times she appeared to lip read and respond to normal vocal commands, but in an inconsistent manner. There was moderate tonsilar and adenoidal hypertrophy. The tympanic membranes showed scarring, but no perforations or fluid was seen.

Laboratory studies revealed the skull films to be normal except for a small calvarium. Urinary screening tests for metabolic defects were all negative.

Dr. William Rice*

The child has had several bouts of otitis media but has never been observed to have fluid behind the tympanic membrane. She had a perforation of one ear in the early part of 1963, and was evaluated by an otolaryngologist in St. Cloud who found no abnormalities at that time.

Dr. Frank Wright**

The main findings are her short attention span, clumsiness, and small head size of 49 cm. There is mild inco-ordination and dysmetria,† indicating some cerebellar disorder, though her stereognosis appears normal. This child represents a mild form of cerebellar dysfunction and intellectual retardation. If a hearing defect is present, it has not been sufficient to explain the picture of mental retardation. An electroencephalogram is not indicated, as there is no history of seizure disorder. In general, electroencephalography in the diagnosis of mental retardation is not particularly helpful, as one third of the children who are mentally retarded have normal electroencephalograms.[1] The small head size probably indicates lack of brain growth and has some correlation with intelligence; however, there is no definitive data on this point. In an anatomical and functional sense, there is a reciprocal relationship between cerebellum and motor cortex for controlling and modulating motor activity.[2] For instance, in children who have cerebellar deficit due to anoxia at birth, cerebellar symptoms generally improve with time, resulting from compensatory mechanism of the cerebral cortex.

In the past, some physicians have felt that hyperactivity was a seizure manifestation,[3] but anticonvulsant drugs have no effect on hyperactivity.

In this child the lack of paroxysmal activity and presentation of consciousness mitigates against diagnosis of convulsive disorder. However, the child could benefit from a trial dose of desoxyn to decrease hyperactivity. In some children with hyperactivity, amphetamine compounds seem to have a paradoxical effect; this can only be judged by a trial use of the drug.

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*Physician, St. Cloud, Minnesota.

**Pediatric Neurologist.

†See Test Your Word Score Page 359.

Dr. Harold Ireton*

On the Stanford-Binet test the child scored 87, indicating her ability within the dull normal range. Her concept of the human figure as measured by her ability to draw a man is average for her age. The mother's report of her general social maturity also indicates an average development in most areas as measured by the Vineland Social Maturity Scale. However, in the area of communication, the mother's report indicates difficulty in graphic representation; her printing is limited to copying and she demonstrates no writing whatsoever.

The above results for intelligence may be functionally too high, as other reports indicate that the child is hyperactive and has easy distractibility. In the testing situation, she was given every legitimate opportunity to perform up to the limit of her ability, as extraneous noise and distracting stimuli were at a minimum. The combined findings of intelligence which approaches the normal range, and the behavior manifestations of hyperactivity, distractibility and excitability, plus the reported motor incoordination suggest that we are dealing with a brain-injured child rather than a mentally deficient one. It would appear quite unlikely that she could perform adequately in a standard classroom situation. It should not be presumed, however, that since her measured I.Q. is misleadingly high and she functions at a lower level, this indicates a poor prognosis for future mental development. Her prognosis is somewhat uncertain, but she has shown apparent advance in the level of intellectual functioning, since her earlier intelligence evaluation, and she displays a friendly, outgoing personality, which should be an aid to her general adjustment.

In evaluating the parents, they both appear reasonably mature in their attitudes toward their child and in recognition of her difficulties. It was felt that the father may have more difficulty in accepting the possibility of a handicapped child and may need some counseling. A joint interview with the parents, including the psychologist, pediatrician and referring physician should be arranged to explore with them the details of the psychological testing.

Dr. Wentworth Quast*

It would be extremely important to know how the child is functioning at the present time in the first grade, as this may give us a better indication of her functioning intelligence. Special classes, particularly a smaller class, would certainly be indicated in the educational environment.

Dr. Frank Lassmann**

A 30-decibel bilateral conductive hearing loss is evident at all frequencies. The function of the sensori-neural (cochlea and 8th nerve) portion of the auditory system was judged to be normal as manifested by a normal response to bone-conducted stimuli. When words were made comfortably loud, she was able to understand and repeat them readily, suggesting a promising

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*Child Psychologist.

**Department of audiology and speech.

Continued

candidacy for hearing-aid amplification or medical/surgical procedures.

Auditory memory span was a shade low, but still measured within the normal range. Vocabulary understanding, measured by a multiple-choice picture identification test, was found to be within her age group (another indirect verification of conductive rather than sensori-neural type of hearing impairment). Voice pitch, voice quality, and loudness were normal. Vowel and diphthong speech sounds were intact, but a number of soft consonant sounds were distorted, especially in final position and when blended with other consonants in pairs. This speech-precision finding was entirely in keeping with the limitations imposed by her hearing problem, but she remained very understandable. Oral speech mechanism was found to be normal with adequate tongue and jaw mobility, adequate diadochokinetic movement in articulators, adequate tongue size and extension forward and side-to-side. The most notable feature of the examination of the mouth was the presence of very large tonsils which raised the question of normal Eustachian tube function. There were no aphasia-type language aberrations.

Examination by an otolaryngologist is recommended for evaluation of the possible need for adenoidectomy and tonsillectomy as well as the possibility of reconstructive surgery of the middle-ear ossicular mechanism, if active middle-ear disease is found to be absent. Otosclerosis is unusual in such a young child and there is no family history of this disease. A primary question would be when such reconstruction, if any, should be attempted.

If surgery is postponed or not indicated and a tonsillectomy produces no appreciable change in her hearing, use of a hearing aid would be immediately recommended. At school, she should be given advantageous seating and placed in a small class in order to function more effectively. Her progress should be watched by the teacher and the speech correctionist.

The Final Recommendations of the Conference are as Follows:

1. Dr. Rice, her family physician, will maintain the primary role in further follow-up and counseling.
2. Recommendation will be made for special classes, preferably in a small group.
3. An otological examination will be obtained at the University of Minnesota Hospitals, and if it is decided that surgery should be postponed, Mr. Martin Kammermeier will arrange for the hearing-aid fitting and adjustment. The possibility of adenoidectomy and tonsillectomy will be discussed if there is found to be fluid in the middle ear.

Robert ten Bensel, M.D.
University of Minnesota
Medical Center

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Opportunity is that which, if you have not thought out what it means, you cannot recognize when it comes. — R & R Magazine

Advances

Infections of the Urinary Tract

Part III — Symptomatology*

WILLIAM J. MARTIN, M.D.**
RICHARD D. WAGONER, M.D.**
Rochester, Minnesota

SYMPTOMS OF infection of the urinary tract are variable and depend largely on (1) the acuity of the process, (2) the bacteria's virulence, (3) the urinary and general resistance of the host, and (4) the presence or absence of underlying uropathy or predisposing disease.

Range of Clinical Manifestations

Manifestations of infection of the urinary tract may be minimal, as in asymptomatic bacteriuria, or they may appear as a fulminating systemic reaction with or without localizing signs. About half of the patients with chronic infections are relatively asymptomatic. Some persistent infections of the urinary tract are associated with antimicrobial-resistant bacteria, but the problem often occurs in patients in whom organisms remain responsive to drugs. This suggests either that the urinary tract is being recurrently contaminated or that there are nidi of bacteria which are not being reached by sufficient concentrations of the drug to ensure their eradication. Pyelonephritis can progressively destroy renal tissue while remaining asymptomatic. An explanation given is that small regions of infection in the kidney, having become localized by surrounding fibrous tissue or cellular reaction, can progressively destroy adjacent nephrons without being large enough to produce fever, pain, leukocytosis, or other manifestations. Another factor may be the persistence of bacteria in pyelonephritic lesions in transitional forms. Persistence of bacteria as transitional forms might explain progression of the disease despite sterile cultures of urine and biopsy specimens when standard media are employed. However, reinfection due to a new strain of organism probably occurs more frequently than relapse of an original infection.

In general, the shorter the duration of the disease, the greater is the likelihood of urinary symptoms. Infections manifested by chills, fever, and toxemia usually are associated with dysuria or pain and tenderness in the flank, directing attention to the urinary tract. However, about 10 per cent of patients with acute infection and systemic reaction lack such urinary symptoms. In the absence of localized signs, it is not uncommon to consider such an infection as a fever of undetermined origin; in patients with such fever, it is worthwhile to investigate the urinary tract for infection as well as for hypernephroma.

Urinary Frequency and Infrequency

While polyuria and frequency of urination usually are considered indicative of urinary infection, infrequent voiding may be the initial manifestation of an obstructive lesion of the lower urinary tract or of a functional obstruction such as a neurogenic bladder, which may be associated with or complicated by urinary infection. Also, although enuresis

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*See Part I and Part II, Minnesota Med, January issue, Page 95, February issue, Page 231.

**Section of Medicine, Mayo Clinic and Mayo Foundation.

frequently is of functional origin, it may be a manifestation of various organic conditions, including such infectious states as chronic pyelonephritis, tuberculosis, and postinfectious contraction of the bladder.

Diagnostic Dilemmas

Acute infections in the renal pelvis may rarely produce erosion into a blood vessel and thereby gross hematuria, which can cause confusion with tumors or cysts when associated with defects on urograms.

The distribution of the dermatomes from which the kidney's innervation originates is in the lower part of the abdomen; therefore nausea, vomiting, reflex ileus, and pain due to such infectious lesions as a septic renal infarct or abscess can be confused with various bowel syndromes. Cortical abscesses on the ventral aspect of the kidneys can both simulate and, by rupture, cause peritonitis. Infections in the right kidney can simulate appendicitis; conversely, retrocecal appendicitis with adherence to the right ureter can cause unilateral right pyelonephritis. Especially in older patients, infections of the left kidney may be confused with diverticulitis coli.

An abdominal mass, especially in a child, demands urologic investigation, since as many as 50 per cent of these masses in children originate from the genitourinary system. The mass may not be associated with symptoms or other clinical signs that identify its origin; if evidences of urinary infection are detected, the infection may be of considerable diagnostic value. The most frequent cause of such an abdominal mass in a child is said to be congenital hydronephrosis, followed closely in frequency by Wilms' tumor.[5] When bilateral abdominal masses are palpable, polycystic renal disease is first suspected. Because an ectopic kidney is occasionally confused with an abdominal mass of another cause, it is important to identify the renal parenchyma before considering more heroic investigation. In many cases, roentgenographic visualization of the urinary tract greatly aids in the determination of the type and location of abdominal masses. In certain cases of urinary infection, contradistinctly, excretory urography may reveal lateral deviation of the ureters indicative of an underlying retroperitoneal lymphoma or other tumor that may not be palpable clinically.

Infection as Causative Factor

Chronic infection of the urinary tract may masquerade as another entity. This possibility should be considered in so-called essential hypertension. The exact interplay of infection, renal potassium loss (or retention of sodium), and hypertension is not known; perhaps any one of them can initiate the others, thus establishing a vicious circle.

Renal disease is said to account for a higher percentage of cases of hypertension in children than in adults.[5] Therefore, hypertension in a child particularly dictates the need for a complete urinary investigation, including pertinent microbiologic procedures. In a patient who is more than 30 years old, the blood pressure is said to be significantly higher in bacteriuric than in nonbacteriuric patients.[1]

Although, as previously noted, the relationship of pyelonephritis to hypertension is controversial, the reported occasional favorable response of hypertension, especially of recent onset, to therapy of the pyelonephritis should encourage search for the disease. It is said that hypertension secondary to pyelonephritis eventuates in uremia or strokes more often, and in congestive heart failure less often than do other forms of hypertension. However, Schreiner[10] noted that congestive heart failure due to intervening hypertension was the presenting syndrome in a number of his patients with chronic pyelonephritis. In some patients, chronic urinary infection may present as malignant hypertension or as encephalopathy with convulsions and rising diastolic pressures, especially when they suffer an acute exacerbation of the infection. Healed and low-grade smoldering types of infection also may produce hypertension. If the process is inactive when the hypertension is discovered, the true nature of the problem may be apparent only to the pathologist.

However, in some patients with hypertension and urinary infection, the infection exists as a secondary phenomenon. If asymptomatic bacteriuria is a relatively latent stage in the natural history of pyelonephritis, long-term studies on the results of eliminating bacteriuria may aid in clarifying its relationship to hypertensive and other diseases.

In such syndromes as uremia of obscure origin, "salt-losing nephritis," and toxemia of pregnancy, the possibility of an underlying chronic infection of the urinary tract should be considered. Jackson[11] stated that pyelonephritis may be the most common cause of uremia. Some investigators believe that chronic pyelonephritis is the most common cause of "salt-losing nephritis." Urinary infections should be considered as possibly causative in suspected cases of toxemia of pregnancy, particularly when proteinuria, pyuria, and hypertension persist for seven days post partum. Asymptomatic bacteriuria is probably associated with an increased incidence of toxemia of pregnancy, but whether its detection and treatment reduce the risk of the complication is unclear. The prematurity and mortality rates for infants born to untreated bacteriuric patients are said to be higher than those for infants whose mothers are nonbacteriuric or have been treated for bacteriuria;[1] but this is disputable.

Infection as Complicating Factor

Since urinary calculi predispose to infection and since one of the ultimate phases of healing in infection of the urinary tract may be nephrocalcinosis, calcification is suggestive of infection. As previously noted, infection of the urinary tract should be considered a complication in certain other underlying abnormalities of the urinary tract or of the host. In this regard, idiopathic retroperitoneal fibrosis (fibrosing retroperitonitis), which is a more recently described entity that usually occurs in men in their early forties, obstructs the lower third of the ureters and is frequently complicated by urinary infections. Lateral deviation of the ureters on excretory urography is suggestive of an underlying retroperitoneal tumor such as a lymphoma, and medial displacement is suggestive of retroperitoneal fibrosis.

Urinary infections in diabetics, especially if oliguria occurs, should bring necrotizing papillitis to mind. Necrotizing papillitis, or so-called renal medullary necrosis, which may accompany chronic pyelonephritis and probably is a consequence of it, occurs much more frequently in diabetics than in nondiabetics. The complication also appears to have been precipitated in such susceptible persons by instrumentation of the urinary tract. The classic description of necrotizing papillitis includes a dramatic picture of sepsis, fever, lumbar pain, massive pyuria, microhematuria, culture of mixed organisms from the urine, uremia, and death. Also, in a classic instance, tissue from the papillae may be found by straining the urine with cheesecloth. However, some patients with necrotizing papillitis have died after a nondescript clinical course, usually in uremia. Bacteremia due to gram-negative bacilli sometimes occurs as a terminal event in these patients.

When certain states such as pregnancy, diabetes, disease or injury of the spinal cord, pelvic relaxation, and prostatism are encountered, urinary infections are likely, since statistically the probability is high and some of these infections are relatively asymptomatic. Although the phenomenon is not as common as it was previously in patients with chronic urinary infection, the physician should beware of possible underlying tuberculosis, especially if the patient has the disease elsewhere; the same applies to brucellosis. Secondary bacterial infection is even more confusing in patients with primary renal disease such as nephrosis or glomerulonephritis.

Other Causes of Urinary Symptoms

Burning sensation on micturition does not always indicate infection. Interstitial cystitis, urethral caruncle, and senile vaginitis may produce dysuria that is not due to urinary infection. Dysuria that continues despite control of infection does not warrant further use of antibacterial agents; use of any of several "bladder sedatives," such as phenylazo-diamino-pyridine hydrochloride (Pyridium) in amounts of 0.1 gm. four times daily, may be helpful, but local treatment of

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the bladder may be necessary. Psychogenic frequency in a patient who recently has had acute infection of the urinary tract can also be confusing.

Less Characteristic Findings

In acute infection of the urinary tract, there are usually no signs of impaired renal function or hypertension such as sometimes occur in acute glomerulonephritis. Hematuria is not characteristic of pyelonephritis and calculus, and tumor and other lesions are considered first. Proteinuria of more than 3 gm. per day is not characteristic of infection and is more suggestive of glomerulonephritis. In urine of low specific gravity, detection of so-called gitter cells suggests pyelonephritis, but such cells are also found in other renal diseases. Some investigators believe that leukocyte casts in the urine sediment are indicative of pyelonephritis.

In certain diabetics, pyelonephritis might directly or indirectly contribute to a decrease in insulin requirements, which may be somewhat surprising since infection often exerts a contrary effect. A theoretic mechanism for decreased insulin requirements in patients with renal disease is one in which the renal parenchyma has a major part in the degradation of insulin; hence a destructive process of any type might cause a corresponding decrease in insulin requirements. Also any debilitating disease, including pyelonephritis, might reduce intake of food sufficiently to result in a decrease in insulin requirements.

Common Indices

The most commonly employed indices of urinary infection are (1) demonstration of persistent bacteriuria, (2) compatible findings on renal function studies, (3) corroborative cystoscopic, pyelographic, and other urologic studies, and (4) positive microbiologic and histologic data on renal biopsy. The degree of renal damage caused by urinary infection usually parallels the duration of the infection rather than the severity of the symptoms. Concentration of urine and results of renal clearance tests help to establish the degree of renal parenchymal damage. If, after fluids are withheld overnight, the specific gravity of the urine is 1.020 or more in the morning, renal function probably is not severely compromised. It appears definite that patients with asymptomatic bacteriuria have an increased incidence of impaired ability to concentrate the urine, elevated levels of blood urea nitrogen, and radiologically demonstrable lesions of the urinary tract. The most common method of testing for vesicoureteral reflux is to fill the bladder with a radiopaque medium, such as 6 per cent sodium iodide, through a small rubber catheter and obtain roentgenograms while the patient is voiding. Numerous refinements of the test are being explored.

Synopsis

Presented synoptically, investigation of the urinary tract, including pertinent microbiologic procedures, should be considered when there is no other apparent explanation for such symptoms and signs as loss of weight, anemia, persistent nausea and vomiting, hypertension, and fever. Atypical abdominal pains, abdominal masses of indeterminate nature, and certain predisposing conditions such as disease or injury of the spinal cord, underlying uropathy, pregnancy, and diabetes mellitus are among the clinical problems that also may prompt consideration of such evaluation.

Infection secondary to stones, strictures, cysts, tumors, and the like may have value as a diagnostic feature of uropathy. Premature intensive use of antibacterial agents without investigation in such cases may eventuate in a diagnostic loss.

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1-11. Published in January issue of *Minnesota Medicine*, Page 99.
11-18. Published in February issue of *Minnesota Medicine*, Page 234.

Progress Note

No Bad Habits: When the patient was asked about his drinking habits, he said, "I never touch a drop of liquor. One quart of brandy lasts all week."

Grand Rounds

Renovascular Hypertension*

The majority of patients suffering from elevation of blood pressure are classified as having what is clinically designated as "essential or idiopathic hypertension." The pathophysiology of this type of hypertension is still a matter of dispute.

Extensive investigations have been undertaken in an attempt to clarify the role of the kidney in the pathogenesis of hypertension, and its ability to affect the peripheral resistance. It is our purpose to briefly review the experimental and clinical aspects of hypertension related to the abnormalities of the renal arteries and kidneys.

The Experimental Aspect of Renovascular Hypertension

The most potent stimulus to the study of hypertension came in 1934, when Goldblatt[1] reported his success in producing hypertension by constricting the renal arteries in dogs. Later he emphasized the many similarities which existed between the chronic and malignant renal hypertension in the dog, and essential and malignant hypertension in humans. The mechanism responsible for the development of experimental renal hypertension is at present unknown. Among the more important theories in this respect are: neurogenic, endocrine, and renal humoral mechanisms.

Most of the recent contributions have dealt with the humoral mechanism, about which the following three distinct views have been postulated: increased production of pressor amines normally metabolized by the kidney but now retained; absence of a renal substance which normally prevents hypertension; and production and liberation into the blood stream of a pressor substance which normally is either absent or not present in sufficient quantities to cause hypertension. Most of the experimental evidence presented to date favors the last view. The latter two hypotheses, however, have led to the classification of renal prival hypertension and renovascular hypertension.

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Renal Prival Hypertension

Grollman[2] studied bilaterally nephrectomized rats and, upon obtaining hypertension, theorized that the kidney is the source of the blood-pressure regulative mechanism which prevents hypertension in normal animals. The same phenomenon was demonstrated in bilaterally nephrectomized dogs when the excretory function was maintained artificially by dialysis and hypertension still supervened as long as the animal lived. Muirhead[3] showed that a kidney homograft restored the renal prival hypertension in the dog to normal level. On the basis of these observations, it was assumed that the hypertension which follows bilateral renal artery constrictions and complete nephrectomy is caused by a single mechanism, namely inhibition of the vasodepressor activity of the normal kidney.

The Renal Hypothesis

In 1898 Tigerstedt and Bergman[4] demonstrated that the renal tissue extract had pressor activity. They called this vasoactive substance renin. Prinzmetal[5] showed that a greater amount of renin was present in the kidneys of dogs with Goldblatt-induced hypertension. This was further substantiated by producing hypertension by transplanting ischemic kidneys into the neck of the normotensive animal, and demonstrating vasoconstricting activity in the renal venous blood from the ischemic kidneys.

Hypertensin

With the discovery of hypertensin, which differed from renin both biochemically and pharmacologically, the concept of "renin-angiotensin" was introduced; the enzyme renin is formed and secreted by the kidney and acts upon the renin substrate, which is an α_2 globulin component of the plasma. The resulting product, angiotensin I, is a decapeptid which is physiologically inactive. A second enzyme is needed in order to convert the inactive angiotensin I into the octapeptid angiotensin II, which is the active vasopressor substance.

Renin

Various experimental data summarized by Tobian[6] seem to indicate that the site of renin formation is the juxtaglomerular apparatus, and suggest that the specific granules of these cells are the renin. The structure of angiotensin is now known; it was recently synthesized by Bumpus and Page,[7] and by Rittel and his associates.[8] It is an extremely potent vasoconstrictive agent. The renin angiotensin pressor system represents the humoral mediator of hypertension caused by the ischemic kidney with the juxtaglomerular cells acting as regulators of renin secretions, by virtue of their sensitivity as "stretch receptors," to changes in arterial flow or pressure. A view differing from the preceding hypothesis is that renin is capable of inhibiting the antihypertensive function of the normal kidney. Therefore it is apparent that the exact mechanism associating the diseased kidneys with hypertension is not clear and none of the current hypotheses is capable of encompassing all the relevant experimental data.

The Clinical Aspects of Renal Hypertension

The clinical counterpart of the above experiments started with the idea presented by Ask-Upmark[9] in 1929 that unilateral renal disease might be related to hypertension. The first report of a successful nephrectomy planned to improve hypertension was published in 1937 by Butler.[10] A considerable number of nephrectomies have subsequently been performed with the hope of curing hypertension. However, since they were not based on solid criteria, the results were generally unsatisfactory. The cure rate at best in published series failed to exceed 26%.[11]

Specific Etiologic Factors

Unfortunately, the majority of patients with hypertension defy specific etiologic diagnosis; they are cured, however, when a specific cause is recognized and treated. Among such causes of hypertensive disease wherein the basic etiology can be determined and surgical therapy effectively employed are: pheochromocytoma, aldosterone adenoma of the adrenal glands, coarctation of the aorta, extra renal vascular lesions, and unilateral renal parenchymal disease amenable to nephrectomy.

Renovascular Lesions

Our present purpose is to consider the subject of renovascular hypertension. The vascular lesions capable of diminishing the renal blood flow include renal artery stenosis, renal arteriovenous fistula, renal artery occlusion, and aneurysms of the renal artery. By far the commonest lesion is renal artery stenosis. Although several different causes of stenosis have been reported, the majority of cases encountered are due, in order of their frequency, to arteriosclerotic changes, fibromuscular hyperplasia, or congenital deformities.

Although the true incidence of hypertension due to renal artery stenosis is not known, the number of cases will increase with the knowledge and high index of suspicion by the individual physician. The diagnosis has been made in all age groups from infancy to the eighth decade of life. The physician's attention should in particular be directed to renovascular hypertension under the following circumstances: hypertension in children and young adults, hypertension of recent onset, hypertension that rapidly progresses to the malignant phase, malignant hypertension, elevated blood pressure in patients with a history suggestive of renal vascular trauma, hypertension in the patient with arteriosclerosis elsewhere in his vascular system, sudden progression of mild hypertension, and hypertension which does not respond to the drugs available.

Diagnosis

The physical examination will not often permit a definitive diagnosis. However, the renal regions should be carefully auscultated for the presence of a systolic bruit. The absence of such a bruit in no way, however, diminishes the possibility of a renal arterial abnormality. In the majority of patients with renal artery stenosis, routine laboratory investigations are usually negative, including the urinalysis and blood urea nitrogen. Chest X ray and electrocardiogram only serve to signify the physiologic importance of the hypertension by demonstrating left ventricular hypertrophy and enlargement. Azotemia may develop in the presence of severe bilateral arterial occlusive disease resulting in renal insufficiency.

Intravenous Pyelogram

The intravenous pyelogram with serial visualizations of the kidneys at

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30 seconds and at 1, 2, 3, 5, and 15 minutes may demonstrate one or many of the following findings: decreased renal size, delayed nephrogram, hyperconcentration of contrast material in the affected kidney, and notching of the pelvis or ureter due to collateral arterial blood supply around the stenotic area.

Radioisotope Renogram

For further evaluation, the following specialized examinations may be carried out: the radioisotope renogram, studies of differential kidney function, and renal arteriography.

The simplest of these is the radioisotope renogram. Following the intravenous administration of radioisotope-tagged Hippuran, the gamma rays can be counted and charted in relation to time. The initial peak of appearance relates directly to renal blood flow and has particular diagnostic importance.

Individual Kidney Study

Howard[12] introduced differential functional studies of the kidneys for the detection of unilateral renal involvement producing hypertension. The same principle was later modified by Stamey. The kidney with significant renal artery stenosis excretes less sodium, and the total urine output of such a kidney is also diminished. This study involves individual catheterization of the ureters and separately collecting samples of urine for volume and electrolyte measurements. Therefore the most impressive data are obtained with unilateral disease where there is an opportunity to compare the two sides. The data provides information about the function of the kidney to be correlated with the deformities demonstrated by arteriography.

Arteriography

Arteriography has been accomplished with reasonable risk and with excellent results. Two methods have been employed; the translumbar aortogram and the retrograde method through the femoral artery. Both methods have their advantages and disadvantages. However, lumbar aortography should not be employed in children. Retrograde technique has the advantage of complete mobility as to the point of injection and patient positioning, but should not be performed in patients with arteriosclerotic changes in the iliac and femoral arteries.

A typical arteriographic finding may be nonfilling of the renal artery, arteriosclerotic narrowing of the artery, fibromuscular strictures or bands, poststenotic dilatation, collateral vessels, and wedging or notching of the renal cortex during the nephrographic phase due to infarction or ischemia.

Therapy

Medical management of such patients never results in permanent cure. In fact, these patients are less responsive to drug therapy than patients with essential hypertension. The surgical management consists of either removing the kidney or repairing the artery. The most desirable procedure, however, is restoration of normal arterial flow for the following reasons: in bilateral disease this is the only method available, renal tissue is preserved, and the kidney supplied by the involved artery may be the better kidney in terms of its parenchyma.

Regarding the last statement, histologic studies from the two kidneys in instances of unilateral diseases have shown significant arteriolar nephrosclerosis on the side without vascular constriction. Because of this, delayed or even incomplete reduction of the blood pressure following an operation may be seen.

Nephrectomy

Removal of the kidney is recommended in the patient with unilateral disease who is a grave surgical risk, and in the management of an anatomically inoperable arterial lesion. Fortunately, these two circumstances are infrequently encountered.

Repair of the Renal Artery

In reconstructing the diseased renal artery, a variety of techniques have been employed. These include endarterectomy with or without the use of a patch; excision of the stenosed segment and reanastomosis; reimplantation of the divided end of the renal artery to the aorta distal to its origin; and finally, a bypass graft from the aorta to the renal artery. The splenic artery has been used to bypass the left renal artery stenosis. The operation is usually performed under hypothermia. A long midline or paramedian incision provides the best exposure, particularly when both arteries are involved. After the exploration of the involved segment, as well as the artery distal to it, pressure measurements are made by direct puncture of the artery proximal and distal to the stenosis. Bilateral renal biopsies should be obtained prior to the reconstruction of the diseased arteries, as they may be of value in the further management of the patient.

Results

The results of the surgical treatment in terms of control of the hypertension in properly selected cases have been gratifying. Sixty to eighty per cent restoration of normal blood pressure has been reported. The return of blood pressure to normal may take place as early as a few hours postoperatively, and as late as several weeks after the operation.

Renal Arteriovenous Fistula

Since the first report of renal arteriovenous fistula producing hypertension in 1928,[12a] approximately thirty more instances have appeared in the literature. The majority of these have had a congenital etiology, with trauma being the most common cause in the acquired group. The presence of a continuous thrill or bruit in the renal area has been common. Aortography usually shows a widely dilated and tortuous renal artery; in addition, prompt visualization of the renal vein and the inferior vena cava confirms the diagnosis. Venous oxygen saturation of blood obtained with a catheter introduced into the inferior vena cava at the level of the renal vein provides further diagnostic information. Relief of the hypertension can be achieved by nephrectomy. Associated renal parenchymal involvement by the fistula precludes direct arterial repair.

Continued

Renal Artery Aneurysm

As of 1959, approximately 150 instances of renal artery aneurysms were reported in the literature.[13] Their over-all incidence is considered to be 1% of all aneurysms. The etiology may be trauma, arteriosclerosis, infection or congenital deficiency in the arterial wall. Most are saccular and occur in the distal portion of the main renal artery or just beyond its primary bifurcation. In all cases reported the incidence of hypertension has been 15-20%. The cause and effect relationship is not clear. Microscopic or gross hematuria has been found in one third of the patients.[14] In addition to hypertension, other complications include renal infarction, rupture, or formation of an arteriovenous fistula. The diagnosis is made by aortography and treatment should usually be surgical, aiming at excision of the aneurysm and at arterial reconstruction, if possible.

Renal Artery Thrombosis

Acute thrombosis of the renal artery may result either from thrombosis of the previously diseased artery or from embolism. Total infarction or ischemia may give rise to severe hypertension which can be fatal. Typically, such acute ischemia is characterized by flank pain, hypertension, and in about 50% of the cases, occult or frank hematuria. Aortography provides the definitive diagnosis. Therapy consists of nephrectomy or direct arterial repair for main renal artery thrombosis, and subtotal resection of the kidney in instances of occlusion of the smaller branches of the renal artery.

Summary

Hypertensive patients fall into two general categories: those where a specific etiology amenable to surgical management can be defined, and a second group where the cause remains unknown. Despite progress in the medical management of the latter group, therapy is not curative. Hypertensive patients are cured, however, when a specific cause can be discovered and eradicated by an operation. Among the commonest of the surgically remediable hypertensive states are renal artery stenosis, renal arteriovenous fistula, renal arterial aneurysm, and renal arterial thrombosis. Patients who are especially suspected of having renovascular hypertension are considered. The manner and rationale of the workup and treatment are reviewed, with emphasis on the role of angiography and surgery. The results of surgical management with proper case selection have been gratifying.

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Mixtures of the Magical and the Practical

Sometimes the witch doctor or the mental healer has used manipulations and even drugs, and the old herb doctor has taken care to gather his plants with a certain ritual or while mumbling spells, and only during certain phases of the moon. Furthermore, the herb doctor has often fallen from grace, scientifically speaking, and has prescribed a drug not because experience showed him that it was useful but perhaps because the astrologers believed that it and the disease to be treated were both under the protection of the same sign of the zodiac. Or perhaps because a walnut looks like a brain with all its convolutions, the old doctor gave powdered walnuts for insanity; or he gave red medicines for anemia and yellow ones for jaundice. Or he shaved elder bark downward to get a cure for vomiting and upward to get a cure for diarrhea!

And so it goes today; the faith healer calls in an obstetrician to help with a difficult case of labor, the spinopath prescribes diet and insulin for a diabetic, and the regular physician cures many a hysterical patient with a combination of pills, impressive apparatus, suggestion, and personal magnetism. (Walter C. Alvarez)*

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*Rapport, Samuel, and Wright, Helen: Great Adventures in Medicine. The Dial Press, New York, 1952, p. 22.

Derivatively Speaking

Influenza derives from the Italian word influenza (influence) and originated when all illness was ascribed to the malign influence of the stars.

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Abstracts, Briefs and Commentaries

GASTROINTESTINAL COMPLICATIONS OF COLLAGEN DISEASES

Apparently intestinal infarction, perforation, and hemorrhage are being observed with increasing frequency in patients with vasculitis, lupus, and dermatomyositis. The difficulties of the surgical management under these circumstances are readily apparent. In view of these problems a study was made of 342 well documented cases of collagen disease from the Henry Ford Hospital.

The over-all instance of gastrointestinal complication was 5.8%, with a 21.1% incidence in polyangiitis, 9.6% in dermatomyositis, and 1.7% in systemic lupus.

Reviewing the types of complications leads the authors to suspect that a common pathogenesis applies to all of them. They believe there is a progressive destruction in small vessels leading to varying degrees of vascular necrosis, which is then followed by infarction, ulceration, hemorrhage, perforation, or varying combinations of these.

The implications of steroid therapy are discussed. Fourteen of the twenty patients developing complications were on steroids at the time. Obviously steroids do not prevent these catastrophes and may actually induce some of them. In some instances they may mask or disguise the severity of the problem.

Management of such complications in patients with collagen disease is a real challenge. In addition to judicious use of all the ancillary measures, surgery should be as prompt, conservative, and rapid as is consistent with an effective procedure.

Fifteen of this series of twenty patients recovered from their complication, but six of the survivors subsequently expired as a result of their systemic illness.

COMMENT: Perhaps the observation of increasing frequency of surgical complications in patients with collagen disorders attests to the increasing efficacy of medical treatment in salvaging these individuals for longer periods of more comfortable living. If this be so, we can anticipate a continuation of these difficult problems until the time when these vascular destructive processes can be reversed or prevented. Such studies as the one presented by the Henry Ford group are most instructive to the average clinician who encounters the problem much more infrequently.

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Couris, G. D., Block, M. A., and Rupe, C. E.: Gastrointestinal Complications of Collagen Diseases. Arch Surg 89:695, 1964.

INCIDENCE OF GALLSTONES

This investigation was carried out to determine the number of patients who developed gallstone disease after gastric resection for ulcer. The only report found in the literature by the investigators, bearing on this subject, was by Bernt, who in 1960 reported 12 cases of gallstone disease in patients who had undergone Bilroth II resection.

The follow-up showed that gallstone disease developed in almost every second patient within nine years after the Bilroth I resection. One hundred forty-eight patients were followed up with cholecystography between one and fifteen years after gastric resection. Only seven of one group of twenty-six had clinical symptoms of gallstone disease.

Gallstone disease was diagnosed in 42 per cent of the patients treated with Bilroth I resection, while the incidence was only 13 to 20 per cent in the Bilroth II group. They conclude that the Bilroth I operation may accelerate the development of gallstones as compared with the Bilroth II operation. Among the cases in which the mean period of 11 years had elapsed since treatment, 24 to 29 per cent of the patients who had undergone Bilroth II resection had gallstone disease.

This is an unusual report and should be of great interest to abdominal surgeons. I personally recall seeing no such report previously. It might be worthwhile to review the postgastric resection records in this country.

Stanley R. Maxeiner, M.D.
Minneapolis, Minnesota

Lundman, T., Orinius, E., and Thorsen, G.: Acta Chir Scand 127:130, 1964.

INSULIN, TOLBUTAMIDE, SEROTONIN, AND THE DUMPING REACTION

In a follow-up of previous observations on the beneficial effect of insulin on the dumping reaction, the authors have studied 33 postgastrectomy patients who had postprandial dumping. The characteristic vasomotor and gastrointestinal symptoms were significantly decreased in 29 of the 33 patients. Most of them were treated with both Orinase and Periactin, the latter being a serotonin antagonist. The level of benefit was not maintained for a consistent or a long period of time in some of these patients; however, the drugs would appear to be a very worthwhile addition for trial in patients who have this distressing problem.

The Orinase was given in .25 to .5 grams five or ten minutes before meals, and the Periactin in 4 to 8 millograms 30 minutes before meals.

J. H. Strickler, M.D.
Minneapolis, Minnesota

Sullivan, M. Bruce, Jr., and Patton, Thomas B.: Insulin, Tolbutamide, Serotonin, and the Dumping Reaction. Ann Surg 159:742, 1964.

FASTING FOR OBESITY

Intermittent facts — 5 to 14 days — in the correction and control of intractable obesity afforded the opportunity for clinical evaluation while the patients lost 0.7 to 1.8 kg. per day. A subjective sense of well-being and lack of hunger was attributed to the hyperketonemia provoked by the fast. Pregnancy, uncontrolled labile diabetes, peptic ulcer, and recent hepatic and myocardial disease were considered contraindications to the total fast. During the fast, water, noncaloric beverages, weak tea, and coffee were allowed. Serum electrolytes, cholesterol, CO_2, fibrinolytic activity, and steroid excretion were normal, although the urinary loss of NaCl exceeded the normal initially. Previously undiagnosed hypertension, diabetes, prediabetes, and cholelithiasis were frequent findings. Fasting reduced all cases of mildly elevated blood pressure to normal. Diets of 1,500 to 2,300 calories daily, with 1- or 2-day fasts at 7- to 10-day intervals, served to reduce the weight further while permitting a more liberal diet on a day-to-day basis.

Courtesy of References and Reviews
Journal of the American Medical Association

Duncan, G., Jenson, W., Cristofori, F., and Schless, G.: Amer J Med Sci 245:515, 1963.

GASTRIC CARCINOMA

One hundred twenty gastric carcinomas which had been operated upon were studied by Nadler and Cabrera from the standpoint of their microscopic classification. A modified Dukes' classification, in which types A, B_1, and B_2 revealed no lymph node involvement, was found to have a better prognosis for survival than types C_1 and C_2 where lymph node involvement was evident.

Total gastrectomy did not offer appreciably any better chance of survival than the subtotal gastric resection, and it was expressed that the procedure which removed the tumor completely, and not the one which would presumably provide the greatest chance for cure, was the procedure of choice.

Twenty per cent of those in the classification for Dukes' A and B had a survival rate of 5 years, while only 4.8 per cent of those in the classification of C and D attained a 5-year survival.

It was suggested that gastric washing be instituted as a routine part of a physical examination in patients over 50 years of age, in order to increase the possibility of discovering cancer at an early and optimal stage of operability.

No comparative diagnostic studies were made in regard to the findings from gastric washings and those of X ray. In this objective study it would appear that any procedure which allows an earlier diagnosis in carcinoma of the stomach should be worthwhile as a routine procedure.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Nadler, Sigmund, H., and Cabrera, Aurelio: Gastric Carcinoma. Surgery 56:334, 1964.

THE SHELTERED WORKSHOP: A FRONTIER FOR MEDICINE

The words "sheltered workshop" sound new and strange in the ears of many Minnesota physicians, yet the best, (and largest) example of such workshops are the Goodwill Industries of Duluth, Minneapolis and St. Paul. Founded in Minneapolis in 1919, Goodwill Industries in these three cities currently employs almost 450 persons for a combined annual payroll of slightly less than one million dollars. The physician's role in the sheltered workshop program demands at the very least an awareness of both definition and scope of this program.

Continued

Including Goodwill, there are now twenty-one sheltered workshops in Minnesota, training 200-300 persons at a cost of $400,000 a year. The blind, deaf, mentally retarded and mentally ill are some of those to whom such training is directed. In addition, the victims of age, epilepsy, cerebral palsy, cardiac disease, and the partially paralysed are eligible for instruction. Training for regular employment is the goal of the sheltered workshop, but the handicapped individual often needs a sheltered work situation at the beginning of his re-educational period, allowing him to adjust both physically and emotionally to his handicap.

The purpose, then, of the sheltered workshop is to provide employment opportunities for the disabled individual unable to obtain work in regular or competitive job situations. Extending the idea of the sheltered workshop to community service is a far-reaching concept. In this instance, where there exists a local demand for temporary or part-time employment, the handicapped person is retained by the workshop as an employee. The employer then pays the sheltered workshop for the service rendered. The workshop provides supervision, prevents exploitation and assumes reponsibility for insurance, tax records, etc. Experience with this plan has been very encouraging.

Not all "trainees" become employable, but experience indicates that about half of those trained are ultimately able to obtain regular jobs. With 3000 to 4000 severely handicapped persons in this state at the present time, the potential value of the program is obvious.

One of the acute problems facing the expansion of the sheltered workshop program concerns the use of the subminimum wage. Legal precedent has been established, allowing the workshop or employer to pay the handicapped individual according to what he can earn in terms of productivity. Thus minimum wage laws may be waived and this has incurred opposition from union organizations and others. However, the subminimum wage is allowed only for the severely disabled, certified as unable to earn a minimum wage. Misunderstood, this provision of the law is looked upon as a social and economic regression. But for the disabled individual, the choice is not that between a minimum and subminimum wage — it is between a subminimum wage and nothing, nothing but illness and frustration. Psychologically, a subminimum wage is at least a foot in the door of self-reliance and independence.

Thus the concept of adding life to years receives added impetus from the sheltered workshop, providing job training, counseling and supervision to those severely disabled persons in our communities. Because this is a health-related facility dealing with the life and happiness of our patients, as physicians we owe it to ourselves to keep abreast of these times.

John V. Thomas, M.D.
Duluth, Minnesota

MANAGEMENT OF ESOPHAGEAL BURN

When esophageal injury from corrosives is established, items of central importance to management are steroid therapy and antibiotics. Prior to starting such therapy, however, a thorough esophagoscopic examination is of the utmost importance. This is particularly true if the program of management includes dilations, and these latter should be reserved for cases in which a tendency to stricture is definitely demonstrated. The authors report on a series of 100 consecutive patients. Of these, 47 were known to have normal esophagi at their last examination. Only 3 patients developed strictures. Except for the initial necessity of tracheotomies on 2 patients on admission, the only complications noted were the occasional development of moon-face. This symptom disappeared one to three months after the steroid was stopped. There were no known significant complications.

Of the 100 patients, 70 were children three years old or younger. The other 30 were over ten years old, and 25 were attempted suicides. The distribution between white and Negro patients was about equal, but there was a high proportion of persons of Latin American extraction in the white group. Solid lye was the noxious agent in 54 per cent, but the administration of water, milk, vinegar, etc., probably liquefied it to some extent in many cases. Most of the burn cases were due to solid or liquid lye, but sulphuric and hydrochloric acid, lysol, and inorganic phosphorus were other causes.

Here is the program outlined for management of lye burns: Steroid and antibiotic therapy are started as soon as an esophageal burn, or a reasonable likelihood of it, is established. (a) Suggested prednisone schedule: First four days, 60 mg. (20 mg. every eight hours) ; next four days, 55 mg. daily (20-15-20) ; next three days, 40 mg. daily (15-15-10) ; next three days, 30 mg. daily (10 mg. every eight hours) ; next three days, 20 mg. daily (5-10-5) ; next two days, 10 mg. daily (5-0-5) ; last two days, 5 mg. daily. (b) Tetracycline while on prednisone therapy. (c) Potassium supplement given orally. (d) Nasogastric tube or string (optional). (e) Esophagoscopy in one week and one month. (f) Chest X ray weekly. (g) Barium swallow at one month. It is believed that the relatively high prednisone dosage during the early stage of the injury suppresses granulation tissue and fibroblastic activity. Children and adults get the same prednisone dosage except in adults who are found to have severe esophageal burns at the initial esophagoscopic examination. Such adults are maintained on 60 mg. prednisone for an additional period of two weeks. Small nasogastric tubes are passed in patients showing evidence of severe oropharyngeal burns or where oral intake of food and fluids is not sufficient. The tube is left in place until soft foods can be swallowed easily. The initial esophagoscopic examination is made within two to five days under general anesthesia both for children and adults. The entire esophagus is examined in order to determine fully the extent of the injury. If at the end of the month of therapy the esophagus is completely normal, the patient is discharged completely, but if any deviation from normal, even mild hyperemia, is found, the patient is seen again two to six months later. If there are severe burns, particularly with granulation tissue, repeat esophagoscopy is done ten days later, with dilations by Hurst bougies if there appears to be narrowing of the lumen.

Courtesy of Medical Abstract Service
Berwyn, Illinois

Cannon, Stanley, and Chandler, J.: Eye, Ear, Nose and Throat 42:35, 1963.

ANGIOGRAPHY IN CURRENT PRACTICE

In this short article the authors discuss the advantages, limitations of angiography, the criteria for patient selection, the principal problems involved with contrast media, catheter methods and noncatheter methods.

Pointed out is the fact that there is no area of the human body that cannot have the blood vessels visualized to demonstrate arteriosclerotic conditions, inflammatory conditions, or neoplastic conditions. In many cases angiography and correlation with laboratory studies can make an exact diagnosis impossible by physical examination methods. In the future the need for study of the vascular system in grafts and organ transplantation is evident. Pointed out is the fact that angiography is a procedure that requires great skill; complications can be minimized by discouraging occasional angiographers. This is especially true in that the arteriographer must know a great number of different techniques which can be selectively fitted to the particular patient. The authors feel that the catheter methods are needed in selected cases but that the noncatheter methods of angiography are more advantageous and cause less difficulty. In conclusion they feel that angiography of any form will be recognized as a routine radiologic procedure that requires co-operation between the radiologist and vascular surgeon.

This excellent short article succinctly gives the clinical indication for angiography. It also points out that the real danger in the technique is not the technique per se but the individual who performs the study. I wholeheartedly agree that angiography is a very specialized field which requires an intense interest and experience. There are numerous institutions and individuals willing to teach the techniques to those physicians willing to learn.

The procedures require a team effort on the part of the radiologist and the vascular surgeon, as complications that occur usually require the services of a vascular surgeon. Therefore, it is my opinion that all procedures should be done as a team.

Jerome T. Grismer, M.D.
Minneapolis, Minnesota

Marshall, T. R., and Ling, J. T.: Angiography — Its Place in Current Practice. Vascular Disease I:3, 1964.

Too Busy to Age

Lincoln wrote of himself as "old and withered" at forty-eight — two years before he was elected President. . . . After that date he did not speak of his age; he was too busy. — Joseph Fort Newton

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He who sacrifices conscience to ambition burns a picture to obtain the ashes.
— Chinese proverb

One of the greatest sources of suffering is to have an inborn sense of honor.
— De Casseres

Book Reviews

First we shall want the pupil to understand, speak, read, and write his mother tongue well. — H. G. Wells

THE CARE OF THE GERIATRIC PATIENT — E. V. Cowdry, Editor, 2nd ed., Saint Louis, C. V. Mosby, 1963. 566 pages, index, references.

Writing both as a gerontologist and a geriatric patient, Dr. Cowdry attempts to fill the gap between abstract studies of the aging process and the care of the aged. As editor, he has compiled a comprehensive manual of geriatric medicine, psychology and sociology by a distinguished group of contributors including Paul Dudley White, Warren Cole and Paul Starr.

The comfort and well-being of the physiologically deteriorating person is the theme. Problems are investigated from the standpoint of the patient and his physician, and of the aging population and its place in the community. Equal space is given to the medical and surgical problems of preventive medicine and specific therapy, to the psychology of the aged and their psychiatric reactions, and to the really major and often neglected problem of the life of the individual in the community. Home-care programs, nursing homes and rehabilitation receive their rightful places.

Designed primarily for physicians, the nontechnical style and comprehensive scope make this manual a valuable tool for paramedical personnel and for social and government agencies concerned with geriatrics.

Extensive bibliographies following each chapter are a ready source for further reading in particular areas of interest.

In the forward, Dr. I. S. Ravdin states that the perplexities of geriatrics are here to stay unless some catastrophic event leads to mass death of those suffering from geriatric disorders; or, through some method not now available to us, "old age" can be prevented or delayed. The authors are to be congratulated for bringing together available knowledge about the aged.

George Kitzmiller, M.D.
Hennepin County General Hospital
Minneapolis, Minn.

THE PROCESS OF EVOLUTION — Paul R. Ehrlick, and Richard W. Holm, McGraw Book Company. Inc., 1963. 347 pages.

This publication follows a well-ordered plan wherein any given chapter is built upon foundations laid down in the preceding chapter. The authors have used the principles of evolution to develop their views on the pattern of interaction of matter.

Beginning with the basic elements found in organic compounds, they build amino acids, nucleic acids, proteins, genes, cells and organisms. After giving a short background of genetic mechanisms, they show how these work to alter populations as their environment changes.

While having no practical clinical application, this book provides a great deal of stimulus to consider individual variation, and the place or purpose of disease processes on populations.

Jean Eckerly, M.D.
Hennepin County General Hospital
Minneapolis, Minn.

THE CIGARETTE HABIT — AN EASY CURE — Arthur C. Cain, M.D., Doubleday & Co., New York

For the habitual cigarette smoker who needs an additional crutch to stop the bad habit, this small pocket-sized paperback provides the interesting details for a "Q-Day," Q for quit, no doubt. It allows the habitue a 21-day guilt-laden period in which he may, like a slave, smoke his loved tobacco but not his usual brand.

The last chapter provides some interesting medical and vital statistics.

This book is written for the smoker, but it can be well recommended by the physician to his patients who have become a slave to their pack.

Carl O. Rice, M.D.
Minneapolis, Minnesota

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Minnesota State Board of Medical Examiners

Are Basic Science Laws Effective?*

I must first briefly review for you our philosophy in Minnesota by telling you of the background of the Basic Science laws passed there in 1927. That was 38 years ago, and there has never been a serious suggestion from any responsible person in the State that they be repealed. Wisconsin has passed the 40 year mark in its Basic Science Laws and still supports them vigorously.

In general, there is no question but what the practice of medicine is on a different plane from that of the other so-called healing arts. It would only take up time to go into this truth at any length. The void between our scientific medical practice and the cultist practice is so deep that only the ignorant and those intentionally misled can fail to see it. Our medical men in Minnesota recognized this fact of life many years ago. They considered a means by which they could maintain our high standards and minimize the inroads of the cultists who were thriving and seemed to be about to flourish to even greater heights. It is pertinent here to quote from an early history of medicine in Minnesota. Back in the territorial days of 1853, when our State Association was founded, "the settlements and the trails, the river fronts and the trading posts of the new Minnesota Territory already abounded in quacks and Indian healers of all descriptions." By contrast, may I call your attention to a few facts about Minnesota today.

The Mayo Clinic, for instance, has just concluded its Centennial Year; the doors of the University of Minnesota Medical School were opened 75 years ago and that event is being celebrated this year; the Mayo Foundation for Medical Education is now 50 years of age — that Foundation being a unique alliance between a great public medical school and a world famous private clinical and teaching facility.

Medical men in Minnesota, recognizing the high level of medical practice, in contrast to the low level of the cults, hit upon the Basic Science concept and in 1927, succeeded in convincing our legislators that a Basic Science Law would help to maintain medical standards and, at the same time, freeze out many of the irregulars engaged in the healing arts. The legislators realized, after it was pointed out to them by the physicians, that Basic Science legislation would actually force the cultists to pay for their own eradication.

Before telling you of the results accomplished by the 1927 action of our legislature, I shall briefly explain our attitude toward the arguments that are commonly heard against Basic Science laws.

In the first place, we do not believe that the creation of a Basic Science Board constitutes any impediment to the operation of medical practice laws. What could the impediment be? All we are doing, actually, is to take six subjects out of the medical examination and put them in a separate examination. Each person who professes to be engaged in healing in the state must pass that examination before he can apply to his particular board for a license to practice in his field. The medical man is required to pass these subjects as part of his regular examination. In the absence of a Basic Science Board, the cultists would determine their own tests of basic knowledge and education. It is painful

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*Presented at the meeting of the Federation of State Boards, February 8, 1965.

to contemplate the sham type of examination that would be given in Basic Science by a cultist board. I am sure their examinations would be as much a fake as are their theories of practice.

Opponents of the Basic Science laws seem to feel that the greatest objection to such laws stems from the fact that a man going to a Basic Science state must acquire a Basic Science certificate. In other words, the objectors feel that Basic Science laws are an obstacle to universal reciprocity. I shall outline my attitude toward this objection in a few brief statements:

1. In my years on the Board, I have never seen a qualified physician, genuinely interested in practicing in our State, who was prevented from acquiring medical licensure because of the Basic Science law. A few delays have been observed, yes — but never a stymie.

2. Our Basic Science laws permit reciprocity between accredited agencies. Surely there can be no objection for Basic Science Boards to recognize this and to grant reciprocity in Basic Sciences on the basis of legitimate medical examinations given by the non-Basic Science State Boards of Medical Examiners. Our Basic Science Board does this in many instances and I think our State Boards should encourage the practice. We have nothing to fear in this regard. The Basic Science laws are as strong as the State Boards that enforce them. There will be no recognition of examinations by unqualified Boards such as those of chiropractors or other cultists in our lifetimes, or the foreseeable future.

3. There are 50 states and half of them have seen fit to enact Basic Science laws. It seems that it would be as reasonable to pass such laws in all the states as to abolish them in all. This would be another way of acquiring uniformity and universal reciprocity, if that is truly desirable.

4. In my mind, universal reciprocity is still a moot question. Does medical licensure in one state indeed give a vested right to practice in another? Surely each state has the right to make its own laws. I have the feeling that general reciprocity would bring about a decided change in the pattern of tenure of physicians in particular locations. In many instances this might not be beneficial or advantageous to the individual, or to the public. Those who experience the need to escape — the need to make a fresh start in another state — frequently do not improve things by moving. Yet I feel that these are just the persons who may change locations and go to a distant state more or less on a whim, or in the hope of magic relief from their difficulties. Strictly enforced, Basic Science laws are more apt to keep such individuals from moving than they are to discourage more desirable practitioners who have legitimate reasons for moving. But, this is unproven ground and it may represent straying from our topic.

Now I shall show a slide summarizing our experiences:

Minnesota Annual Registration

	1928	1963	Increase
Physicians	3442	8681	5239
Chiropractors	493	539	46

I leave it up to this audience to decide on the effectiveness of Basic Science laws in our State.

J. P. Medelman, M.D.
Secretary-Treasurer

If you cannot make light of your troubles, keep them in the dark.
— Sunshine Magazine

To become an optimist close one eye and believe with the other.

The more you say, the less people remember. — Francois Fenelon

Medical Economics

FOR OUR ELDERLY:

WILL IT BE MEDICARE
OR
WILL IT BE ELDERCARE?

A new eldercare program, superior in all respects to the King-Anderson, the so-called Medicare plan, has been introduced in Congress.

Representatives A. Sidney Herlong, Jr., (D., Fla.) and Thomas B. Curtis, (R., Mo.) are the authors of the proposed legislation which would cover payment of physicians' care, surgical and drug costs as well as hospital and nursing home care.

The introduction of the Herlong-Curtis Eldercare Bill (H.R. 3727) represents a breakthrough of historic importance to all citizens in the drive to provide people over 65 with a wide range of health care to meet their individual needs.

This bill is the best piece of legislation dealing with the health care needs of the elderly now before Congress. Careful analysis of H.R. 3727 indicates that it will assure more benefits at less cost to the taxpayer, than any other measure for people 65 and over who need care and can't afford to pay for it. It provides for sound financing and experienced administration. The tested machinery of the established insurance systems, including Blue Cross and Blue Shield and health insurance companies would be used.

Doctors Support New Eldercare Proposal

The medical profession recently recommended and now supports wholeheartedly the principles embodied in the Herlong-Curtis eldercare proposal.

Details of the Doctors' Eldercare Program were announced to the public on January 9, 1965, by Doctor Donovan F. Ward, President of the American Medical Association. Eligibility for benefits under the Herlong-Curtis, physician-backed eldercare proposal would be determined quickly before illness strikes — and without a welfare department type of investigation.

Persons over 65 would qualify for a medical care policy submitting a simple statement of income.

Medicare Means More Taxes

The Herlong-Curtis Eldercare Proposal would be financed by federal-state matching funds through an extension of a Kerr-Mills program that already exists.

The Medicare tax plan would call, by con-

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trast, for higher payroll taxes on all wage earners to pay benefits for everyone over 65 — the rich as well as the needy. The tax burden would fall heaviest on those least able to pay. For example, the $5,600-a-year worker would be forced to pay as high a tax as the $56,000 executive. Here is a detailed question-and-answer explanation of the various issues involving medical care for older people.

Q. What is the Kerr-Mills Law and how does it work?

A. The Kerr-Mills law was passed by Congress in 1960. The law enables the individual states to guarantee to every aged American who needs help the health care he requires. In addition to the more than 2,000,000 covered by Old Age Assistance, the law is designed to benefit all other older persons who are ordinarily self-supporting but unable to meet the cost of a serious or prolonged illness. It helps those who need help. Each state can pattern the program to meet its own particular needs. It is administered locally where the individual needs of the aged are known. By helping *only* those who need help, it avoids waste of tax dollars. It is financed by federal-state matching funds and is being implemented as rapidly as most federal-state programs.

Kerr-Mills In Minnesota Has Splendid Record

Q. Does Minnesota have a Kerr-Mills Law?

A. Yes. Implementing legislation was passed by the 1963 legislature. The program became effective July 1, 1964.

Q. Who is eligible for Kerr-Mills benefits in Minnesota?

A. Applicants must be 65 or over and must have an established abode in a given county of Minnesota. If temporarily absent from the state the applicant must still be deemed a resident.

Q. Must applicants be paupers to receive Kerr-Mills benefits?

A. Definitely not. In Minnesota a married couple is allowed an annual income of $2400. An applicant for MAA and his spouse may have equity in real property up to $15,000 plus liquid assets of $1,000. For an individual the annual income limit is $1800, the real property limit is $15,000 and liquid assets can be no greater than $750.00. These do not include personal and household effects, or a prepaid burial plot, or the cash surrender value of each person's life insurance up to $1,000.00.

Q. What is the financial responsibility of Minnesota Kerr-Mills applicants?

A. The individual applicant, or he and his wife together, must have spent or obligated himself or themselves to spend $200.00 on health care during the preceding 12 months. (Health Insurance premiums can be included in this "deductible" amount). *All* benefits from any private health insurance must be applied first to the cost of any recipient's care before he is eligible for Kerr-Mills benefits.

Kerr-Mills Offers Generous Benefits

Q. What type of benefits does the Minnesota Kerr-Mills program provide?

A. The Minnesota Kerr-Mills implementation provides *total health care,* in the hospital, nursing home, doctors' office, patient's home, clinic, or diagnostic center. It covers surgery, drugs, dentist care, appliances, ambulance service, home nursing, rehabilitation, necessary laboratory services, preventive care, and immunizations. There is no time limit to the benefits. They continue for the duration of the illness.

Q. How is the Minnesota Kerr-Mills program administered?

A. The regulations are promulgated by HEW and Minnesota Department of Public Welfare. Actual case work is performed by local County Welfare Board.

Q. How is the Minnesota Kerr-Mills program financed?

A. The federal government provides 56.4% of the health care dollars expended and 50% of the actual administrative cost of the program. The remaining 43.6% is divided 50-50 between the state and county.

Q. Must Minnesota Kerr-Mills applicants sign a lien?

A. No. The federal Kerr-Mills act does not permit liens.

Q. How many Minnesotans have received help under the Kerr-Mills Law?

A. After five months of operation, approximately 12,500 persons have received benefits. In November, 1964, an average payment of $206.02 had been made for each of the 11,754 recipients. The Department of Public Welfare originally estimated the monthly cost at $225.00 per patient.

Q. Will more people be assisted under the plan?

A. Yes, the Department of Public Welfare feels that the caseload will stabilize at about 18,000 recipients for the ensuing year. Approximately 140,800 people could be covered by the benefits.

Q. How much does the Minnesota plan cost?

A. For the 1964-65 fiscal year, the state legislature appropriated $7,650,000. A like amount was to be matched by the 87 counties. The federal reimbursement at the present time is 56.42 per cent of the total cost. A spokesman for the Department of Public Welfare has stated that "our utilization and expenditures have not been as great as we expected." Currently expenditures are 12-15% under original estimates.

Medicare Offers Many Questions — Few Answers

Q. What is *Medicare* (in contrast to Eldercare)?

A. Medicare is a system of compulsory hospital insurance for elderly persons financed through the Social Security system. The King-Anderson Bill, a proposal now before Congress, is an example of the compulsory approach to Eldercare.

Q. Who would be eligible for Medicare benefits?

A. All persons over 65 who are currently receiving Social Security cash benefits or benefits under the Railroad Retirement Act. All persons who could receive Social Security cash benefits except that they are continuing to work and are earning self-support incomes. All who, before 1968, have attained or will attain the age of 65 and who are not covered by Social Security or Railroad Retirement Benefits. All who, after 1968, will have worked for at least three quarters on a Social Security covered job for each calendar year elapsing after 1965 and before the year in which they attained age 65.

King-Anderson Benefits Are Limited

Q. What benefits would the present version of the King-Anderson Bill provide?

A. 1. Limited Hospital Care — Up to a 60 day stay in a semi-private room in a hospital during a benefit period, after the current per diem rate for one day is paid. The per diem rate is about $40.00-$44.00.

2. Limited Post-Hospital Services — Up to 60 days per benefit period in a hospital-affiliated post-hospital facility. This can be a nursing home, but the patient must be transferred from a hospital before he can qualify and the nursing home must provide 24-hour nursing service, supervised by a registered professional nurse, and it must have and use a utilization review plan.

3. Home Health Services, including 120 visits in 1966; 240 visits in any calendar year after 1966. Visits may include nursing care under supervision of a registered nurse, physical, occupational, or speech therapy, etc. Home health care can be furnished only by persons working for tax-exempt public or private non-profit organizations.

4. Outpatient Hospital Diagnostic Services including 30 consecutive days after paying one-half of the current per diem rate for one day. The per diem rate is about $40.00-$44.00.

Q. What benefits would be excluded from the King-Anderson Bill?

A. Surgery; doctor's care, at home, at the office, or in the hospital; medicine, drugs, etc., furnished outside of approved hospitals or convalescent homes; dental care; outpatient therapy, eye glasses, wheelchairs, crutches, and other health appliances.

Medicare Tax Would Whittle Pay Checks

Q. How would taxpayers pay for Medicare?

A. The federal government will create a new payroll deduction tax called the Federal Hospital Insurance Trust Fund. In addition to paying Social Security taxes, federal withholding taxes and state withholding

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taxes out of one's paycheck, all workers covered by Social Security will pay a new "Medicare" tax. Together, employees and employers will pay .6 of 1% of the first $5600 earned income for the new tax. This will increase until 1969 when the tax rate will be .9 of 1% of the first $5600 income. The self-employed will begin by paying .45 of 1% of $5600 and by 1969 the rate will be .675 of 1%.

Q. How much would the Social Security tax be increased to pay for Medicare?

A. The new rate will be based on $5600 a year income. In 1966, the tax paid by employees and employers each would be increased from the present $174 per year to $238. The tax on a self-employed individual would be increased from $258.20 to $358.40. In 1971 and thereafter, the tax on the employee and employer each would be increased from the presently scheduled $222 per year to $291.20. The presently scheduled tax of $331.20 on a self-employed individual would be increased to $436.80.

	Self-Employed		Employer-Employee (each)	
	Present	Proposed	Present	Proposed
1966-1967	6.2%	6.4%	4.125%	4.25%
1968-1970	6.9%	7.5%	4.625%	5.0 %
1971 & thereafter	6.9%	7.8%	4.625%	5.2 %

Eldercare — Medicare Differences Are Great

Q. How would the doctors' new eldercare plan differ from Medicare?

A. The doctors' eldercare program would provide a wide range of medical care for over-65 Americans needing financial help in meeting illness costs, including payment for physicians' care, including surgical and drug costs, as well as hospital and nursing home charges. Compare these wide-ranging benefits with the "medicare" tax proposal which offers a restricted number of days in a hospital or nursing home, plus limited outpatient care, all of it amounting only to an estimated 25 per cent of the usual cost of an illness. Under the doctors' program, care would be related to individual needs.

Q. How would the protection offered by the doctors' eldercare program be financed?

A. The doctors' eldercare program would utilize Blue Cross and Blue Shield plans and health insurance companies, assuring experienced administration. Policies would be available to protect the elderly from illness costs. Purchase of the policies would be financed entirely, or in part, by state-federal matching funds, depending upon an individual's ability to pay. These companies and non-profit organizations are already set up. They have the experience gained in providing health insurance protection to millions of Americans. The program would utilize an established insurance system. It would not undermine the system, as medicare would, through unfair government competition.

Q. How would needy persons apply for aid under the doctors' plan?

A. By filing a simple statement of income with the appropriate state agency. Those with incomes below, or within, limits set by the states would automatically become eligible for benefits. Those reporting incomes lower than the state's lowest figure would receive paid up policies from the public funds. Those with incomes between the minimum and the higher limit set by the states would have part of their insurance charges defrayed from the matching fund pool, on a sliding scale. The higher the income, the less would be paid by government. Thus, the degree of need would be the measure of the amount of financial help received.

Q. How would the doctors' eldercare plan be administered?

A. The medical profession is hopeful that the program would be administered by state health departments, the logical arm of government to handle health problems. This would be authorized under the proposal. Thus, the knowledge and administrative experience of both health officials and insurance carriers could be utilized, without a welfare type investigation.

Q. Would a new federal program be necessary?

A. The machinery already exists in the Kerr-Mills act for providing federal help to the states on a matching basis to assure the aged the health care they need. Only a few simple amendments to Kerr-Mills and existing state laws would be necessary to put the doctors' plan in operation; that is, legislation (1) providing for a simple income declaration; (2) utilizing the private carriers in providing the help, and (3) permitting administration of the program to be placed under the state health departments.

Public Would Benefit From Herlong-Curtis Proposal

Q. How would this benefit the public?

A. By taking advantage of a program that is already in existence and operating, the doctors' plan would avoid the necessity for creation of a costly, new federal bureaucracy to administer a centralized program from Washington. By providing aid on a basis of need, the doctors' plan would assure that both federal and state dollars were being used to provide care where it is most needed. Available resources would be concentrated on bringing hospital and medical care to those unable to pay for it. Millions would not be squandered on new payrolls, or on financing care for the self-supporting and the well-to-do so that no one could receive more than partial care at best.

Q. What would be the function of the federal government under the doctors' plan?

A. The federal government would provide funds to help the states pay the premiums for those who need help. Historic relations between the states and the federal government would be preserved, with maximum authority and responsibility remaining with the states to guard the interests of their own citizens instead of delegating the responsibility to a central authority in Washington. With the experience of private insurance companies, and of the Blue Cross and Blue Shield plans at the service of the program, a more efficient use of public money would be possible.

MD's Plan Would Not Affect Freedom of Medicine

Q. How would the freedom of medicine be affected?

A. Under the doctors' plan, as under Kerr-Mills, the federal government would have no reason to intervene in the practice of medicine. The Secretary of Health, Education and Welfare, for example, would *not* be required to have "agreements" with hospitals, or be empowered to audit personal medical records in connection with paying the hospital or nursing home bills for beneficiaries of a federal program. An elderly patient would *not* be limited to seeking care in those institutions, only, which are eligible by law or under the Secretary's regulations to participate in a federal program. Protected by his insurance policy, he would retain his freedom of choice.

Q. Would the doctors' eldercare program require any increase in payroll taxes?

A. The Doctors' Eldercare Program would not require a burdensome payroll tax increase on the nation's workers and employers. It has been estimated that the "medicare" tax program, furnishing benefits to *everyone* over 65, the wealthy included, would soon cost $5 billion a year. While costs of the doctors' program have not been calculated, it is reasonable to assume they would be substantially less than the "Medicare" tax program, even with greater benefits. Costs of the doctors' program would be subject to factors unknown at this time — for example, the minimum and maximum levels of income to be established by the various states for eligibility. The doctors' program would be limited to those who need help and a portion of the elderly who would qualify would contribute part of the cost themselves. These factors would minimize costs.

Harold W. Brunn, Executive Secretary
Minnesota State Medical Association

Though one may conquer a thousand men a thousand times in battle, he who conquers himself has the more glorious victory. — Buddha

---

He is the best physician who knows how to distinguish the possible from the impossible. — Herophilus B.C. 300

the problem: diabetic . . . overweight . . . unresponsive to diet alone

the answer: "...if dietary control seems to be unsatisfactory . . . [and] if the patient is overweight . . . our first choice is phenformin [DBI] since this is the only oral hypoglycemic agent commercially available at present which does not promote fat deposit."[1]

"...with phenformin [DBI] there may be less preferential stimulation of fat synthesis in the obese, diet-resistant diabetic, favoring both blood sugar and body weight control."[2]

to manage the stable adult diabetic who is overweight and unresponsive to diet alone

DBI® DBI-TD

tablets 25 mg. **timed-disintegration capsules 50 mg.**

BRAND OF PHENFORMIN HCl

DBI together with a proper diet usually affords effective control in the overweight ketoacidosis-resistant diabetic . . . reduces high blood sugar and elevated serum insulin levels, and encourages gradual weight loss toward normal.[3] For the ketoacidosis-prone diabetic, however, insulin is still the essential hypoglycemic drug.

side effects: Gastrointestinal, occurring more often at higher dosage levels, abate promptly upon dosage reduction or temporary withdrawal. precautions: Occasionally an insulin-dependent patient will show "starvation" ketosis (acetonuria without hyperglycemia) which must be differentiated from "insulin-lack" ketosis which is accompanied by acidosis, and treated accordingly. Lactic acidosis has been reported in nondiabetics and diabetics treated with insulin, with diet, and with DBI. Question has arisen regarding possible contribution of DBI to lactic acidosis in patients with renal impairment and azotemia and also those with severe hypotension secondary to myocardial or bowel infarction. Periodic B.U.N. determinations should be made when DBI is administered in the presence of chronic renal disease. DBI should not be used when there is significant azotemia. Any cardiovascular lesion that could result in severe or sustained hypotension, which may itself lead to development of lactic acidosis, should be considered cause for immediate discontinuation of DBI at least until normal blood pressure has been restored and is maintained without vasopressors. Should lactic acidosis occur from any cause, vigorous attempts should be made to correct circulatory collapse, tissue hypoxia, and pH. **contraindications:** Severe hepatic disease, renal disease with uremia, cardiovascular collapse. Not recommended without insulin in acute complications of diabetes (metabolic acidosis, coma, severe infections, gangrene, surgery). pregnancy warning: *During pregnancy, until safety is proved, use of DBI, like other oral hypoglycemic drugs, is to be avoided.* Consult product brochure for full information.

1. Faludi, G.: J. Am. Med. Women's Assoc. 18:722, 1963. 2. Weller, C. et al.: Scientific Exhibit, A.M.A., June, 1962. 3 Moss, J. M. et al.: Medical Times 92:645, 1964.

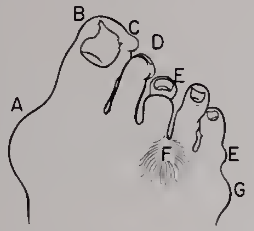
U. S. VITAMIN & PHARMACEUTICAL CORP. • 800 Second Avenue, New York, N. Y. 10017

Special Article

Foot Surgery

Kenath Sponsel, M.D.
Minneapolis, Minn.

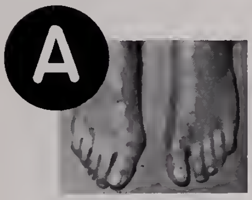
FUNDAMENTAL FORE FOOT SURGERY



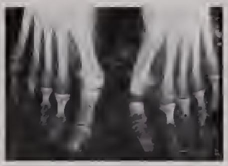
- A Keller Bunionectomy.
- B Ingrown Toe Nail, Border Excision.
- C Nail Removal - Partial Amputation.
- D Tenotomy for Hammer Toe.
- E Ostectomy for Claw Toe and Callus.
- F Neurectomy for Morton's Toe.
- G Ostectomy for Bunionette

See examples to right — Top Row.

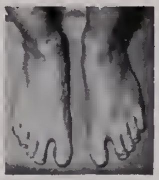
BUNIONECTOMY - KELLER ARTHROPLASTY



I YEAR AFTER LEFT KELLER OPERATION



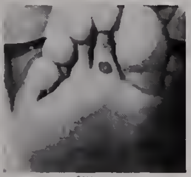
KELLER TYPE RESECTION *CONSIDERED EXCELLENT!*



BOTH CORRECTED SAME PATIENT.

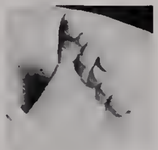
BASICALLY IS RESECTION OF PROXIMAL 3/8" OF PROXIMAL PHALANX AND REMOVAL OF MEDIAL PROMINENCE ON METATARSAL HEAD.

THINGS TO EXCISE



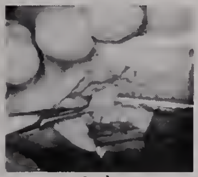
Case

MOLE ON SOLE



Case 2

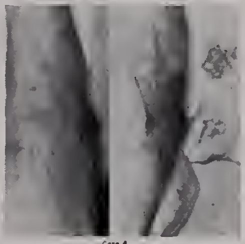
CUTANEOUS FIBROMA



Case 3

GANGLION OF PLANTAR FASCIA

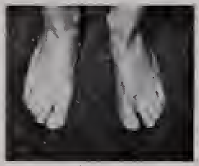
Note: TRANSVERSE INCISION DISTAL TO WEIGHT BEARING AREA



Case 4

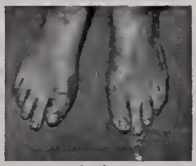
GANGLION OF PERONEAL TENDONS. SURGICAL REMOVAL. WALKING CAST.

BUNIONECTOMY



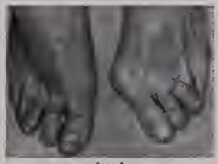
Case 1

Left Keller Operation



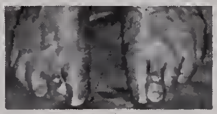
Case 2

Excessive Resection of Proximal Phalanx. Function Improved by Arthodesis



Case 3

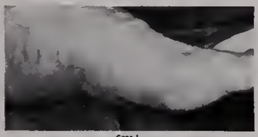
This Man Wore Big Shoes. Did Not Want Operation.



Case 4

75 yr. old Woman Having Severe Hallux Valgus — Rx - Keller Operation, & Adductor Transplant to 1st Met. Head.

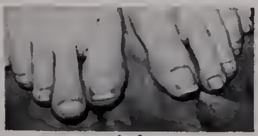
AVOID SURGERY



Case 1

PLANTAR FIBROMA

OFTEN ASSOCIATED WITH DUPUYTREN'S CONTRACTURE IN HANDS.
RECURRENCES AFTER EXCISION TRY HYDROCORTONE INJECTIONS

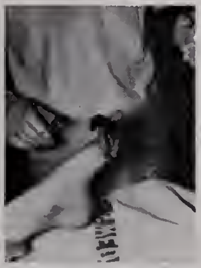


Case 2

GIGANTISM

SURGERY ONLY IF INTERFERING WITH FOOT WEAR.
CAUSE OF CONDITION UNKNOWN

TRAUMA - Mower Injury



Amputated Big Toe

PREVENTION IS BEST!

(buy a reel type mower)

80,000 Injuries per Year with Rotary Mowers.

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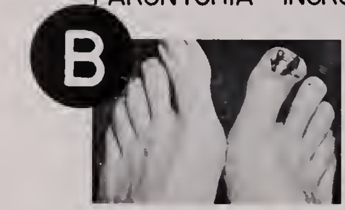
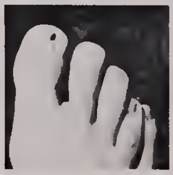
*This exhibit was shown at the A.M.A. — Atlantic City, June 1963.

The purpose of these illustrations is to show interested surgeons what they might do to help ailing feet — and to show interested physicians what surgery of the foot can accomplish.

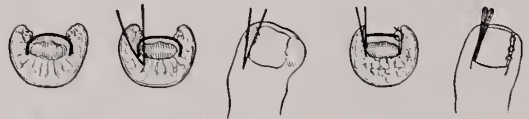
PARONYCHIA-"INGROWN TOENAILS"

B


PRE-OP
5 MONTHS INCAPACITY

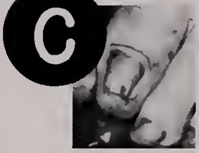

POST-OP-4 MOS.
RUNNING CROSS COUNTRY

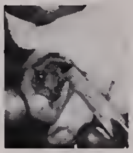
SURGERY — EXCISION OF LATERAL NAIL BORDERS —

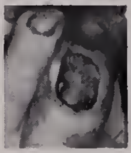

CONDITION EXCISE "V" CUT OUT ALL OF NAIL BED TO BONE & FIBER LOOSELY SUTURED OR FURACIN PACK

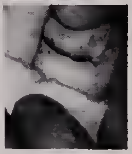
ONE OPERATION FOR PAINFUL DEFORMED GREAT TOE NAILS

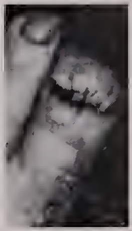
C

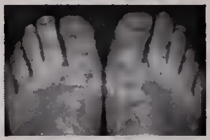

TO REMOVE ALL NAIL & MATRIX


DOWN TO BONE

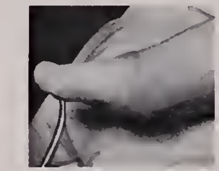

FREE TUFT OF PHALANX

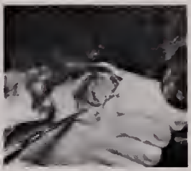

REMOVE 3/8" OF TUFT

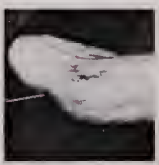

CLOSURE

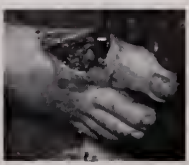

EARLY P.O. RESULT
NO RECURRENCES
RELIEF OF PAIN

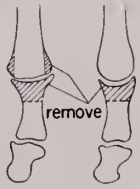
HALLUX RIGIDUS


Case 1
Painful Dorsiflexion and limited motion.


Arthrosis

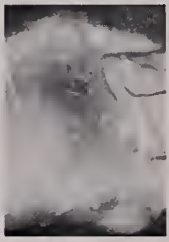

Case 2
℞ Arthrodesis
(One Solution)


Case 3
℞-Resection Proximal Part Proximal Phalanx
(Alternate Solution)



Keller Operation

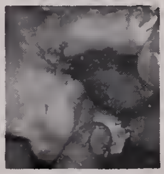
SURGICAL LESIONS


Case 1

Osteomyelitis

I Year Duration in Non Diabetic Patient.
Problems: Infection Originating in Plantar Callus Spread to Dorsum

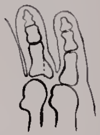
℞ Open Sequestrectomy and Bone Excision.


Case 2

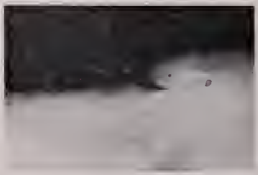
Soft Callus

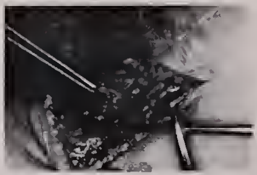
Sites: Usually Between 4th and 5th Toes with Callus on 4th Toe.

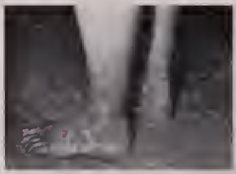
℞: Wider Shoes Highly Successful.
or
Resection of Underlying bone 4th Toe - Proximal Phalanx.

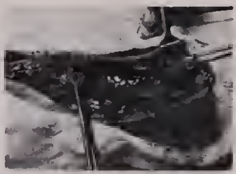


DIVISION-TENDO-ACHILLES

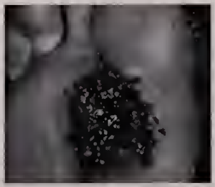

ACUTE

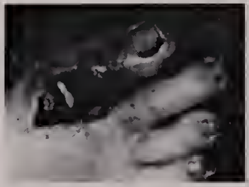

Case 1
REPAIR - CAST 6 WEEKS

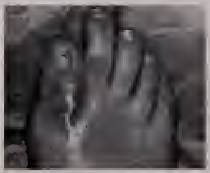

LATE RECOGNITION OF RUPTURE


Case 2
TENDON ENDS CLAMPED GASTROC FASCIAL REPAIR
(Bosworth Method)

GUNSHOT WOUND


Wound of Exit Before Debridement


Wound of Entrance Ten Days After Debridement and Open Packing

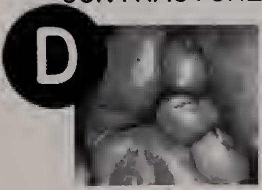

Final Result

- Spike of bone removed from proximal phalanx to permit toe shortening.
- Secondary closure of sole of foot.
- Healed for service, 5 weeks.

The top row shows simple procedures that will alleviate a large percentage of conditions. Most surgeons can master these.

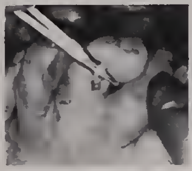
The lower two rows are more complex problems in which the orthopedist is versed.

HAMMER TOE CONTRACTURE OF DISTAL JOINT

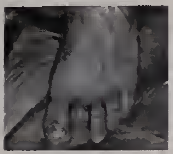


Painful Nail Bed
Callus on Tip

Case 1

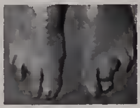


(One Method)
Tenotomy-Long Toe Flexor
Capsulotomy - Distal Joint



Case 2

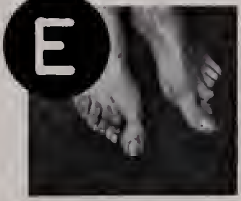
(Alternate Method)
Amputation of Distal Phalanx & Painful Toe Nail

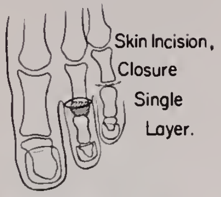


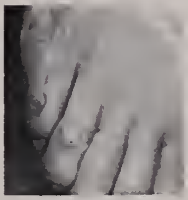
Case 3

Poor Treatment by Toe Amputation. Other Toes May Drift Out of Alignment.

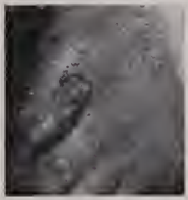
CLAW TOES-RIGID JOINTS





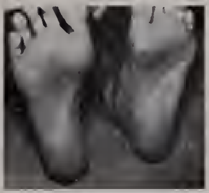


Avoid Callus With Incision

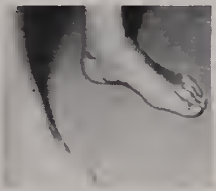


Resect Distal Portion of Proximal Phalanx

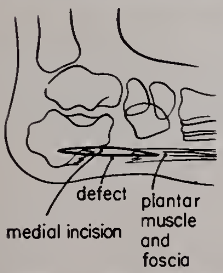
CAVUS FEET - SUPPLE JOINTS



Note: Tight Fascia



High Arch, Calluses on Heel and Ball of Foot.

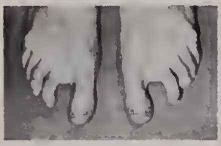


"Technic"

Steindler Plantar Stripping.

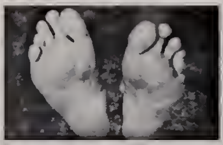
- Medial Approach.
- Fascia and Muscle Origin Stripped From Os Calcis.
- Foot Manipulated Post-Op, Rt. Angle
- 6 wks. Short Leg Cast.
- 6 mos. Night Cast Bi Valved.

CLAW TOES - FLEXIBLE JOINTS



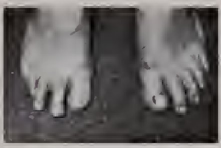
Case 1

Example



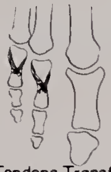
Case 2 - Pre-Op

Associated Metatarsal Callus



Case 2 Post Op

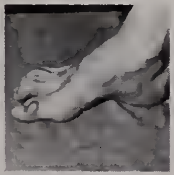
℞ Transfer of Sublimis and Profundus to Proximal Phalanx



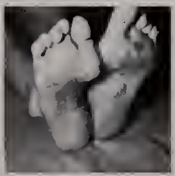
Flexor Tendons Transferred to Flex Proximal Phalanx

CAVUS FEET RIGID JOINTS

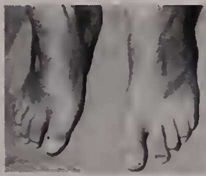
(Example)



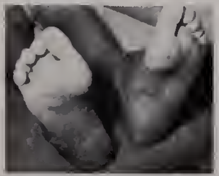
PAINFUL - PRE OP



POOR WEIGHT BEARING



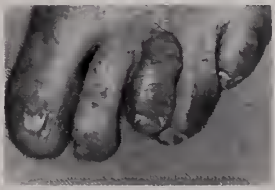
RELIEVED - POST OP
TARSAL WEDGE OSTEOTOMY



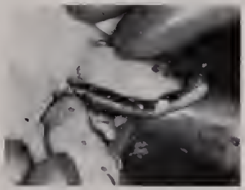
DISAPPEARANCE OF CALLOSITIES

CLAW TOE - HAMMER TOE ℞ - SYNDACTYLISM

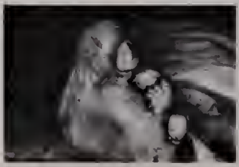
(Example)



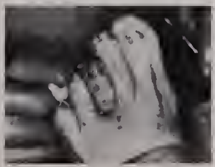
Failure - Resection Proximal Part Proximal Phalanx



Partial Amputation of Painful Fourth Toe



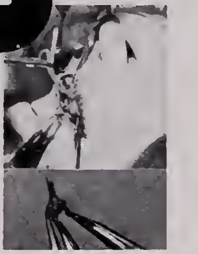
Repair By Syndactylism

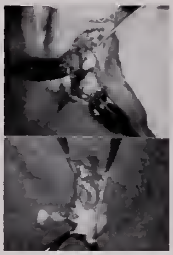


Kelikian

F

PLANTAR NEUROMA
Morton's Toe



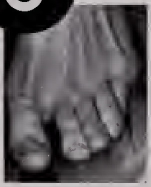


SYMPTOMS – Burning, Cramping, Hypesthesia Usually Between Third and Fourth Toes.

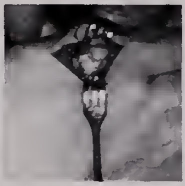
CORRECTION – *EXCISION* – (neuroma)

G

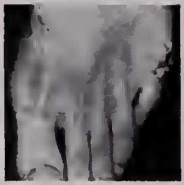
BUNIONETTE – FIFTH TOE



PAINFUL



INVOLVES METATARSAL HEAD

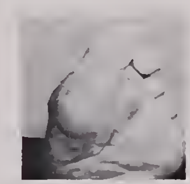


SCAR AVOIDS PRESSURE AREA

BEAUTIES

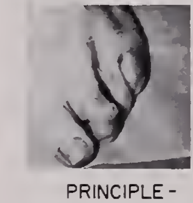
GOOD RELIEF-BUNIONETTE REFUSED BUNIONECTOMY——

PLANTAR CALLOSITY-INTRACTABLE TO ℞

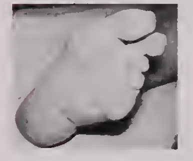


CALLUSES TOO TENDER FOR SHOES

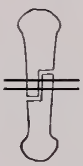
A Case Before and After



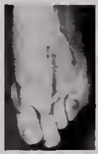
PRINCIPLE – RELIEVE PRESSURE



RESULT: CALLUSES GONE NO ℞ TO CALLUSES

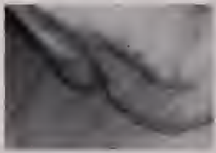


OSTEOTOMY TEMPORARILY HELD WITH KIRSCHNER WIRE



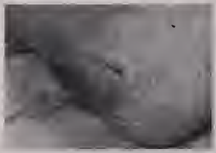
2nd METATARSAL SHORTENED BY STEP-CUT OSTEOTOMY TENDON TRANSPLANT TO CLAW TOE

BONY PROMINENCE-CALLUSES REMOVE UNDERLYING BONE

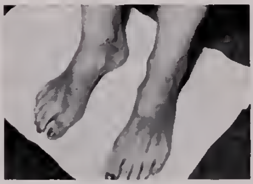


OS CALCIS

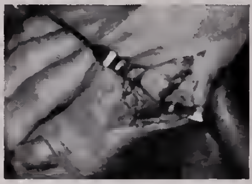
Case 1



AVOID PRESSURE AREA

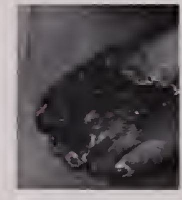


ACCESSORY SCAPHOIDS



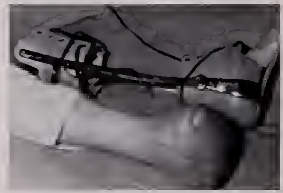
SIMPLE OSTECTOMY FOR BUNION WITHOUT VALGUS

DIABETES-PARTIAL AMPUTATION

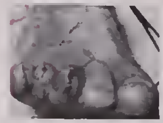


Crush Injury Gangrene

Case 1



Disarticulation Anterior Talus, Os Calcis SQ. Tenotomy Achilles to prevent Equinus

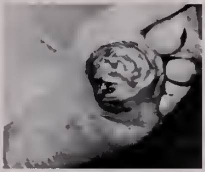


Note: Vertical Incision Preserving Greatest Length of Arteries.

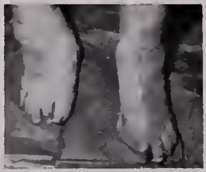
"Technic"

- Sharp Dissection with Minimal Handling.
- Longitudinal Pin-Os Calcis, Talus and Tibia During Healing.
- Suction Drainage.
- Padded Cast Immobilization During Healing.

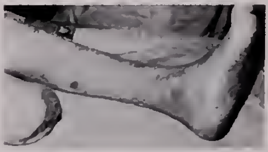
DIABETES-CELLULITIS-ARTHROPATHY



INFECTED BLISTER LATER HEALED

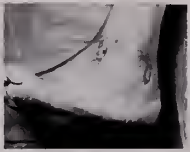


BILATERAL CHARCOT JOINTS (NEUROPATHIC JOINTS)



ONE FOOT AMPUTATED FOR HEMATOGENOUS OSTEOMYELITIS

Case 3



THE OTHER FOOT INFECTION ARRESTED THROUGH DRAINAGE AND PROLONGED CAST

History of Medicine

William Clowes (1540-1604)

That the times produce the man has been irrefutably demonstrated throughout history — but nowhere so patently as in medical history. When challenge arose, it was met!

One such notable challenge was the treatment of gunshot wounds which, in England's centuries of almost unremitting warfare, presented multifarious problems unfamiliar to surgeons prior to the discovery and use of gunpowder.

One of the men who met the challenge was William Clowes, a 16th-century English army surgeon, whose wide observation and practice with soldiers wounded in battle resulted in the work, "Proved Practice for Young Surgeons," used as a reference and text by students.

With what ingenuity and skill Clowes solved one troublesome problem is described in Parker's "Early History of Surgery in Great Britain:"

"In 1573 a soldier named Giles was shown him, who had been wounded three years previously in Flanders by a bullet entering the left iliac fossa. There was still a deep sinus there, which was seriously affecting his health, and the situation of the bullet could not be determined. Clowes made futile efforts to reach it by long probes. He then enlarged the orifice, introduced sponge tents, and even caustics, but he was still unable to get a flexible probe down to find the bullet. He bethought himself that a liquid might penetrate, and injected through a long tube a solution containing alum and sublimated silver, leaving it in while the patient was kept in a suitable position. Twenty-three hours after, pain and swelling began in the right buttock near the anus, which was poulticed. Next day he cut down on the swelling, found the bullet there, and removed it. After a series of dressings and injections the wounds healed up completely."*

Clowes, however, was not the only pioneer in the field of battle injuries; there were others. One might almost say that during her military history England produced a new breed of men — her military surgeons. Instigated by a drive to meet a new and compelling challenge, these men present convincing historical substantiation for the materialistic conception of history: the theory that the times produce the man.

---

*Parker, G., M.A., M.D., M.R.C.S.: The Early History of Surgery in Great Britain. A. & C. Black, Ltd., London, 1920, p. 76.

We all have something to fall back on, and I never knew a phony who didn't land on it eventually. — *Wilson Mizner*

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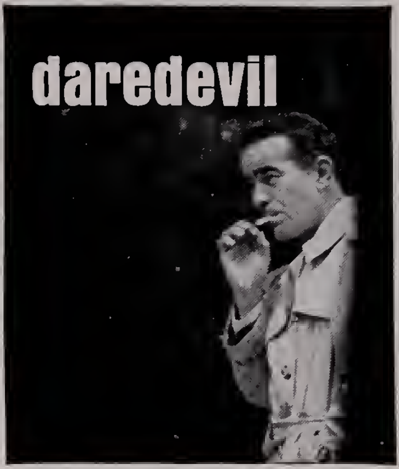

Doesn't think of himself as the reckless type at all. But he goes on taking the *big* risk. Clings to a habit which causes 100 deaths every day from lung cancer and which contributes to many, many more from coronary artery and respiratory diseases. Studies show that the death rate from lung cancer alone for cigarette smokers (one-pack-a-day or more) is 10 times higher than for nonsmokers.

Nobody says it's easy to stop. But living *that* dangerously often winds up in not living at all.

american cancer society
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Give them
a Faith
to live by

Worship this week

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in peptic ulcer therapy—"little things mean a lot"

it's the sum total of many subtle advantages that makes glycopyrrolate a superior anticholinergic

ROBINUL® FORTE glycopyrrolate 2 mg. per tablet

ROBINUL®-PH FORTE

glycopyrrolate 2 mg. / phenobarbital 16.2 mg. / (warning: may be habit forming)

The remarkable efficacy of Robinul (glycopyrrolate) in the treatment of peptic ulcer cannot be attributed to any single characteristic of the drug. Rather it is the sum total of several subtle pharmacologic advantages that enables this anticholinergic to make such a significant contribution to the total ulcer regimen.

Epstein[1] found glycopyrrolate's intensive antisecretory action to be exemplary. Breidenbach[2] was impressed by its pronounced antispasmodic effects. And Young and Sun[3] reported that a 2 mg. oral dose "did not affect gastric emptying or intestinal transit time. . . ." According to Slanger[4], the absence of annoying side effects is an important plus factor ". . . for it permits ready individualization of dosage for control of mild to severe symptoms." Posey[5] sums it up when he says, "In effect, with glycopyrrolate, one approaches an ideal agent for the management of peptic ulcer. With it a vagolytic effect may be obtained without interfering with gastric emptying—the medical equivalent to vagectomy plus an adequate drainage procedure."

We invite you to try Robinul (glycopyrrolate) in your practice. Discover firsthand how several subtle advantages add up to make it the superior anticholinergic agent.

BRIEF SUMMARY

INDICATIONS: In addition to its primary indications for duodenal and gastric ulcer, glycopyrrolate is indicated for other G-I conditions which may benefit from anticholinergic therapy. Robinul-PH Forte (glycopyrrolate 2 mg. with phenobarbital) is indicated when these situations are complicated by mild anxiety and tension.

CONTRAINDICATIONS: Glaucoma, urinary bladder neck obstruction, pyloric obstruction, stenosis with significant gastric retention, prostatic hypertrophy, duodenal obstruction, cardiospasm (megaesophagus), and achalasia of the esophagus, and in the case of Robinul-PH Forte, sensitivity to phenobarbital.

PRECAUTIONS: Administer with caution in the presence of incipient glaucoma.

SIDE EFFECTS: Dryness of the mouth, blurred vision, urinary difficulties, and constipation are rarely troublesome and may generally be controlled by reduction of dosage. Other side effects associated with the use of anticholinergic drugs include tachycardia, palpitation, dilatation of the pupil, increased ocular tension, weakness, nausea, vomiting, headache, dizziness, drowsiness, and rash.

DOSAGE: Should be adjusted according to individual patient response. Average and maximum recommended dose is 1 tablet three times a day: in the a.m., early p.m., and at bedtime. *See product literature for full prescribing information.*

Also available:
Robinul® (glycopyrrolate 1 mg. per tablet)
Robinul®-PH (glycopyrrolate 1 mg. per tablet)
phenobarbital 16.2 mg.
(warning: may be habit forming)

REFERENCES: 1. Epstein, J. H.: Am. J. of Gastroent., 37:295, March, 1962. 2. Breidenbach, W. C.: Investigative Clinical Report, March, 1961. 3. Young, R., and Sun, D. C. H.: Ann. N. Y. Acad. Sc., 99:174, Feb., 1962. 4 Slanger, A.: Journal of New Drugs, 2:215, July-Aug., 1962. 5. Posey, E. L., Jr.: Am. J. Dig. Dis., 7:863, Oct., 1962.

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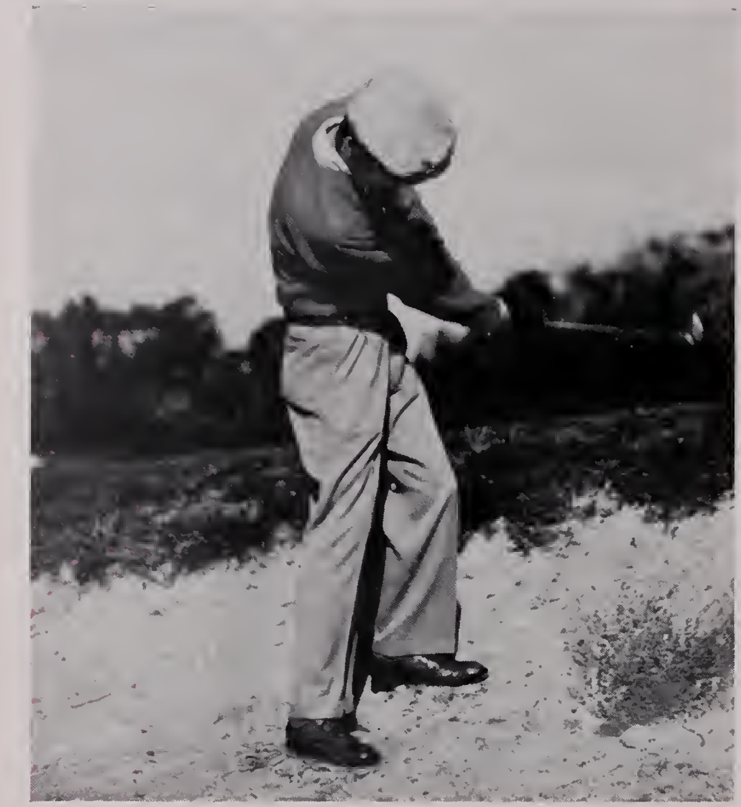

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rational combination therapy for most patients with strains and sprains: relaxes muscle, relieves pain

Also available as 'Soma' Compound with Codeine: carisoprodol 200 mg., phenacetin 160 mg., caffeine 32 mg., codeine phosphate 16 mg. (Warning: may be habit-forming.)

(Warning: Codeine may be habit-forming.) **Indications:** 'Soma' Compound and 'Soma' Compound with Codeine are useful for relief of pain and stiffness in traumatic, rheumatic and other conditions affecting muscles and joints. **Contraindications:** Allergic or idiosyncratic reactions to carisoprodol, phenacetin, or codeine phosphate. **Precautions:** *Phenacetin*—With long-term use, give cautiously to patients with anemia and cardiac, pulmonary, renal or hepatic disease. May damage the kidneys when used in large amounts or for long periods. *Caffeine*—Not recommended for persons extremely sensitive to its CNS stimulating action. *Codeine phosphate*—Use with caution in addiction-prone individuals. *Carisoprodol*—Carisoprodol, like other central nervous system depressants, should be used with caution in patients with known propensity for taking excessive quantities of drugs and in patients with known sensitivity to compounds of similar chemical structure, e.g. meprobamate. **Side effects:** Drowsiness, lightheadedness, dizziness, and gastric complaints have been reported infrequently for either or both of these preparations. *Phenacetin*—Side effects are extremely rare with short-term use of recommended doses. Prolonged ingestion of overdoses may produce dyspnea, cyanosis, hemolytic anemia, skin rash, anorexia, subnormal temperature, insomnia, headache, mental disturbances, and tolerance. *Caffeine*—Side effects are almost always the result of overdosage. Average doses may rarely cause nausea, nervousness, insomnia, and diuresis. Excessive dosage may produce, in addition, restlessness, nervousness, tolerance, tinnitus, tremors, scintillating scotomata, tachycardia, and cardiac arrhythmias. *Codeine phosphate*—Possible side effects are nausea, vomiting, constipation, and miosis. *Carisoprodol*—The only side effect reported with any frequency is sleepiness, usually on higher than recommended doses. An occasional patient may not tolerate carisoprodol because of an individual reaction, such as a sensation of weakness. Other rarely observed reactions have included dizziness, ataxia, tremor, agitation, irritability, headache, increase in eosinophil count, flushing of face, and gastrointestinal symptoms. One instance each of pancytopenia and leukopenia, occurring when carisoprodol was administered with other drugs, has been reported, as has an instance of fixed drug eruption with carisoprodol and subsequent cross-reaction to meprobamate. Rare allergic reactions, usually mild, have included one case each of anaphylactoid reaction with mild shock and angioneurotic edema with respiratory difficulty, both reversed with appropriate therapy. In cases of allergic or hypersensitivity reaction, carisoprodol should be discontinued and appropriate therapy initiated. Suicidal attempts may produce coma and/or mild shock and respiratory depression. **Dosage:** Usual adult dosage of 'Soma' Compound or 'Soma' Compound with Codeine is one or two tablets three times daily and at bedtime. **Supplied:** 'Soma' Compound, orange tablets, each containing carisoprodol 200 mg., phenacetin 160 mg., and caffeine 32 mg. 'Soma' Compound with Codeine, white capsule-shaped tablets, each containing carisoprodol 200 mg., phenacetin 160 mg., caffeine 32 mg., and codeine phosphate 16 mg. Narcotic order form required. *Before prescribing, consult package circular.*

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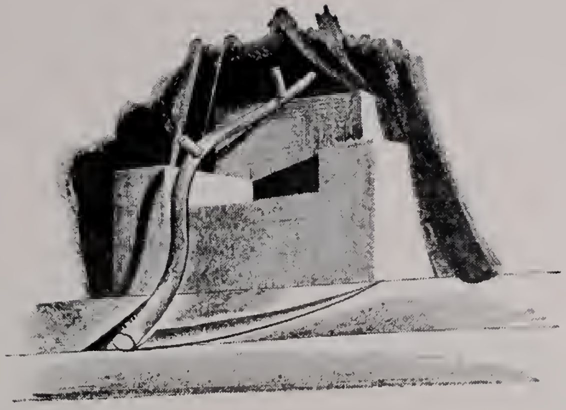

In Memoriam

A dislike of death is no proof of the want of religion. The instincts of nature shrink from it, for no creature can like its own dissolution. — But though death is not desired, the result of it may be, for dying to the Christian is the way to life eternal. — W. Jay

DALE D. TURNACLIFF

Dr. Dale D. Turnacliff, 76, of St. Paul, died December 29th. He had maintained a private medical practice and had worked as medical director of the former Twin City Rapid Transit Company for thirty-six years until his retirement from the post in 1948. Dr. Turnacliff had offices in the Minneapolis Medical Arts building where he specialized in dermatology.

He was born in Waseca County and graduated from the University of Minnesota medical school. He was a member of the Hennepin County Medical Society and the American Medical Association and an associate and 50 Club member of the Minnesota State Medical Association.

He is survived by his wife, a daughter, and a son, Dr. Robert D. Turnacliff, Palos Verdes Estates, California.

J. ANTHONY MALERICH

Dr. J. A. Malerich, 73, St. Paul surgeon, died January 16th. Born in Arlington, Dr. Malerich had practiced medicine in Richardton, North Dakota, Shakopee, Caledonia and fifteen years in West St. Paul before he retired in 1958.

He was a member of the American Academy of General Practice, American Medical Association, Ramsey County Medical Society, an associate fellow of the International College of Surgeons, and an associate member of the Minnesota State Medical Association.

Dr. Malerich is survived by his wife, three daughters, and a son, Dr. J. A. Malerich, Jr. of West St. Paul.

OTTO W. YOERG

Dr. Otto W. Yoerg, 78, retired Minneapolis surgeon, died January 27th. He was a graduate of the University of Minnesota Medical School and a member of the staff of Northwestern hospital for forty years. He was chief surgeon for many years for the Milwaukee Road; Rock Island Lines and Chicago Great Western Railway Co. and a former president of the Minneapolis Surgical Society. He was also a member of the American College of Surgeons and the Academy of Medicine.

Dr. Yoerg was a member of the Hennepin County Medical Society and American Medical Association and a 50 Club and life member of the Minnesota State Medical Association.

He is survived by his wife.

CARL G. BURTON

Dr. Carl G. Burton, 70, prominent St. Paul East Side physician, died January 18th. He was born in Ljungby, Sweden, and came to St. Paul in 1914. He was a graduate of the University of Minnesota Medical School.

Dr. Burton was on Bethel college's board of education for seventeen years, was recently made an honorary member of the Mounds Park Hospital, was a member of the Ramsey County Medical Society, American Medical Association and an associate member of the Minnesota State Medical Association.

He is survived by his wife, and two sons, one of whom is Dr. J. Richard Burton of St. Paul.

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Meetings and Announcements

Choose the company of your superiors whenever you can have it; that is the right and true pride. — Chesterfield

MARCH

Minnesota Academy of Medicine, Regular meeting — March 10, 7:00 p.m., Town & Country Club, St. Paul.

St. Louis County Medical Society, Executive Comm. — March 11, 6:00 p.m., Regular meeting — 8:00 p.m., St. Mary's Hospital, Duluth.

Ramsey County Medical Society, Business & Program — March 29, 8:00 p.m., 15th Floor Lowry Medical Arts Bldg., St. Paul.

Mayo Clinic and Faculty of Mayo Foundation Clinical Reviews, March 15, 16 and 17 and March 22, 23 and 24. Mayo Civic Auditorium in Rochester. Contact: M. G. Brataas, Secretary, Mayo Clinic in Rochester.

Twenty-eighth Annual Meeting of the New Orleans Graduate Medical Assembly, March 8, 9, 10 and 11, Roosevelt Hotel in New Orleans, La. Details may be obtained at the Office of Assembly, 1430 Tulane Avenue, New Orleans, La. 70112.

American College of Surgeons and graduate nurses, in Seattle, March 8-11, Olympic Hotel and Palomar Theatre. Contact: College at 55 E. Erie Street, Chicago.

American College of Physicians golden anniversary session, March 22-26, Conrad Hilton Hotel in Chicago. Contact: College at 4200 Pine Street, Philadelphia, Pa.

University of Colorado postgraduate course in medical technology, March 15-20, in Denver. Contact University, 4200 East 9th Avenue in Denver.

Sixth Annual Congress of the Professions, March 26-27, Pantlind Hotel, Grand Rapids, Michigan. Contact: Helen Menton, 120 West Saginaw Street, East Lansing, Michigan.

Department of Otolaryngology, College of Medicine of the University of Illinois at the Medical Center, Chicago, postgraduate course in laryngology and bronchoesophagology, March 29-April 10. Write: Department at 1853 West Polk Street, Chicago.

APRIL

AMA second annual congress on environmental health problems, April 26-27, Drake Hotel, Chicago. Write: AMA-Chicago.

American Society for Study of Sterility, April 2-4, Jack Tar Hotel, San Francisco, California. Write: W. H. Robertson, M. D., 2700 Tenth Avenue South, Birmingham, Alabama.

Minnesota Obstetrical & Gynecological Society — 9:00 a.m., St. Luke's Hospital, Duluth.

St. Louis County Medical Society — Executive Comm. — April 8, 6:00 p.m., St. Luke's Hospital, Duluth, Regular Meeting — 8:00 p.m., St. Luke's Hospital, Duluth.

Minnesota Academy of Medicine — Regular meeting — April 8, 7:00 p.m., Town & Country Club, St. Paul.

American Academy of General Practice-Scientific Assembly — April 12-15, San Francisco.

Ramsey County Medical Society — Business & Program — April 26, 8:00 p.m., 15th Floor Lowry Medical Arts Building, St. Paul.

Thirteenth Annual Clinical Meeting of American College of Obstetricians and Gynecologists, April 5-8, Civic Auditorium, San Francisco. Write: The College, 79 West Monroe Street, Chicago.

American College of Surgeons ninth postgraduate course in trauma, April 28, 29, 30 and May 1. John B. Murphy Memorial Auditorium, 50 East Erie Street, Chicago. Write: John Fahey, M.D., 1791 Howard Street, Chicago.

National Association of Recreational Therapists, University of Wisconsin, Madison, April 4-9. Write: B. L. Smith, 500 Newton Rd., Iowa City.

Industrial Medical Association, Americana Hotel, Bal Harbour, Fla., April 5-8. Write: Clark D. Bridges, 55 E. Washington, Chicago 2.

ANNOUNCEMENTS

Part II examination will be conducted by the American Board of OB-GYN at Edgewater Beach Hotel in Chicago, April 26-May 1. Applications will be accepted in the office of the secretary during April and May. Contact: Clyde Randall, 100 Meadow Road, Buffalo, N. Y.

®

Of 1,088 patients with confirmed skin and soft-tissue infections... 1,036 or 95.2% were treated successfully with Signemycin®

Note:
Morador et al.* obtained *excellent results in the treatment of 185 out of 191 soft-tissue infections,* all due to staphylococci. They state: "In the most serious infections occurring in patients with impaired resistance (mainly diabetics) we have had very good results in the control of the infectious condition." In these studies, incision and drainage were employed where indicated.

Condition	No. of Patients	No. Responded To Signemycin
Abscesses, various	35	34
Abscess, gluteal or perianal	54	52
Burns, infected	331	307
Carbuncles and furuncles	125	122
Cellulitis	104	102
Lacerations and wounds, infected	142	128
Ulcers, infected	107	106
Various superficial infections	190	185
Totals	1,088	1,036 (95.2%)

---

*Morador, J. L. et al.: Antibiot. Ann. 1959-1960:716.

consistently effective...often when others fail

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tetracycline HCl, 167 mg.; oleandomycin as triacetyloleandomycin, 83 mg.

capsules (250 mg.)

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Brief Summary and Bibliography follow.

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WANTED: Two general practitioners who are interested in general medicine and obstetrics to associate with a small group in west central Wisconsin. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE — 286, 496 Lowry Medical Arts Building, St. Paul, 55102.

WANTED: full-time industrial physician for East Central Iowa industrial plant — excellent opportunity. General practitioner preferred, salary open. Immediate opening. Write: MINNESOTA MEDICINE — 299, 496 Lowry Medical Arts Building, St. Paul, 55102.

WANTED AT ONCE — A general practitioner for fine equipped office, 25 bed hospital, Eventide Home and Nursing Home. Call 427-3515 collect or write: Albert W. Steinle, Box 577 Mountain Lake, Minnesota.

PRACTICE FOR SALE. General practitioner. Will practice for six months with prospective buyer to acquaint him with patients. All new equipment from BMR to X ray. See 20-30 patients daily. Reasonable and terms. Dr. A. H. Wolf, 3145 Hennepin Avenue South, Minneapolis, 55408.

EK-2 Burdick excellent condition, rolling stand. Not more than 200 recordings made. Asking $500. Will accept best offer. Owner in residency training. Call 724-7823 or Radiology Department, VA Hospital PA 9-2381, Minneapolis.

MORGAN, MINNESOTA, Wants General Practitioner — Present Physician retiring after 33 years. Opportunity to take over well established practice. Progressive community in the best rural area of Southern Minnesota. Office space and equipment available. Call or write John Hageman, Pharmacist, Morgan, Minnesota. Telephone Morgan No. 96.

PEDIATRICIAN — to head pediatric department of expanding prepaid medical specialty group; Minneapolis-St. Paul; excellent beginning salary; opportunity for teaching and professional pursuits; liberal vacation and benefits. Alfred F. Anderegg, M.D., Medical Director, 2500 Como Avenue, St. Paul 8, Minnesota.

BURNSVILLE MEDICAL CENTER — office space for one, two or group of physicians in Twin Cities fastest growing suburb — ideal for second office. Call Minneapolis 890-1434 or St. Paul 698-8618.

WANTED: General practitioner by established three-man group in own building, fully equipped. Southwestern Minnesota — county seat — population 3,500. New hospital — fine churches — good schools, public and parochial. Golf club — grass greens. Hunting and fishing. Starting salary with opportunity for partnership. No initial investment necessary. Write: MINNESOTA MEDICINE — 199; 496 Lowry Medical Arts Building, St. Paul 55102

WANTED: An energetic general practitioner for a permanent position in our new clinic. Salary open. Age under 35 years. Partnership agreement negotiated at eighteen months. Scheduled post graduate and vacation periods. New modern medical-dental clinic with full diagnostic facilities at Highway 100 and Wayzata Blvd. in suburban Minneapolis. Large established family practice with opportunity for surgical privileges. Contact: Alton C. Olson, M.D. or Richard E. Anonsen, M.D., 5 West Lake Street, Minneapolis. TA 7-4711.

OPPORTUNITY for general practitioner to join long-established three-man clinic in excellent county seat community of 7,000 in Western Minnesota. Newly expanded quarters with new equipment and furnishings. New hospital and two new rest homes. Attractive salary. Full partnership in three years with no financial investment. Write: MINNESOTA MEDICINE — 300, 496 Lowry Medical Arts Building, St. Paul.

WANTED: Internist to join well-established five-man group in town of 10,000 located in progressive area having good living conditions. Call or write: Alex Shadid, M.D., CA 5-2511, Elk City, Oklahoma.

TWO G. P.'s NEEDED — Northern Minnesota county seat; new hospital; office space available; two other physicians in town; anesthetist on hospital staff; good schools; all churches; excellent hunting and fishing; housing available; full details upon request. Contact: Administrator, Roseau Area Hospital, Roseau, Minnesota.

WANTED: OB-Gyn in well-established group in city of 15,000. Good hunting and fishing, we have over 1,000 lakes in county. Excellent hospital and clinic facilities. Write: V. I. Hanson, Business Manager, Park Region Medical Center, Fergus Falls, Minnesota.

WANTED: Internist, board eligible or certified to join established internist in Western Minnesota community. Write: 617 7th Avenue West, Fergus Falls, Minnesota.

WANTED: General practitioner at Kerkhoven, 110 miles west of Twin Cities, approximately 5,000 patient load, fully equipped clinic; two accredited hospitals within 16 miles; new high school; fine churches; excellent farm area at edge of lake country. Contact: Kenneth Peterson, 234-5151, Kerkhoven, Minnesota.

Continued to page 422

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SIGNEMYCIN®

Side Effects: Glossitis and allergic reactions, as well as severe anaphylactoid reactions, have been reported as rare side effects. Should significant reaction or idiosyncrasy occur, discontinue medication and institute countermeasures. Use of tetracycline during the last trimester of pregnancy, neonatal period and early childhood may cause discoloration of developing teeth. Reduce usual oral dosage and consider serum level determinations in patients with impaired renal function to prevent possible liver toxicity due to excessive accumulation of antibiotic in the serum.

Precautions: Overgrowth of nonsusceptible organisms may occur. In such cases, discontinue medication and institute appropriate specific therapy as indicated by susceptibility testing. Aluminum hydroxide gel given with antibiotics has been shown to decrease their absorption and is contraindicated. The coloring agents used in Signemycin Syrup and Pediatric Drops may produce red discoloration of stools.

Triacetyloleandomycin, a constituent of Signemycin, administered to adults in daily oral doses of 1.0 Gm. (3 Gm. Signemycin) for periods of more than ten days may produce hepatic dysfunction and jaundice. In the rare patient who requires this high dosage level of Signemycin initially, liver function should be carefully followed and dosage should be reduced, as promptly as possible, to the usual recommended range of 1.0 to 2.0 Gm. per day. Therefore, Signemycin is recommended primarily for the treatment of acute or severe infections, with treatment restricted to a ten-day period. If clinical judgment dictates continuation of therapy beyond ten days, serial monitoring of the liver profile should be carried out, including BSP, transaminase, and cephalin flocculation tests. Changes observed in liver function were reversible following discontinuation of the drug.

Formulas: Capsules: 250 mg. Signemycin (167 mg. tetracycline HCl and 83 mg. oleandomycin as triacetyloleandomycin).

Capsules: 125 mg. Signemycin (83 mg. tetracycline HCl and 42 mg. oleandomycin as triacetyloleandomycin).

Syrup: 125 mg. Signemycin (tetracycline equivalent to 83 mg. tetracycline HCl and 42 mg. oleandomycin as triacetyloleandomycin) per 5 cc.

Pediatric Drops: 100 mg. Signemycin (tetracycline equivalent to 67 mg. tetracycline HCl and 33 mg. oleandomycin as triacetyloleandomycin) per cc.

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Note:

The high rate of response to Signemycin in these cases is noteworthy because the totals include many patients with difficult-to-treat infections, many whose infections had proved resistant to other agents, and many who had been treatment failures on other therapy.[1-87] In addition the following criteria were used for the cases cited: (1) only published results were used (2) results were confirmed by clinical and/or laboratory findings (3) patients were cured, not "improved" (4) dosage conformed with current recommendations in the United States (5) no other anti-infective agents were used concomitantly (6) no instance of prophylactic use was included in these tabulations.

Condition	No. of Patients	No. Responded To Signemycin
Ear, nose and throat infections	507	465
Respiratory infections	1,028	954
Gastrointestinal infections	425	387
Genitourinary infections	748	684
Skin and soft-tissue infections	1,088	1,036
Bone and joint infections	71	64
Deep-seated or generalized infections	257	251
Obstetrical & gynecological infections	341	320
Miscellaneous conditions	592	570
Totals	5,057	4,731 (93.5%)

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GENERAL PRACTITIONER WANTED: Lamberton, Minnesota. Nearly new Sears Roebuck Foundation designed clinic available. Excellent school, churches and community. Call or write: Wallace Nelson, Lamberton, Minnesota, 56152, Telephone 752-7717.

WANTED: Associate for a general practice, leading to partnership. Previous partner entered specialty training January 1st. Position available anytime. Excellent working conditions. Salary open. Contact: C. R. Peluso, M.D., 938 Lowry Avenue N.E., Minneapolis.

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MEDICAL CLINIC: Completely equipped air-conditioned medical clinic including X ray. Has seven examining rooms, X-ray room and lab. Two offices, waiting room, dental clinic including lab. Brick building 70x45 on ground level. An excellent St. Paul-Minneapolis location. Will sell or lease with option to buy. A great opportunity. Call or write: Birney J. Novotny, CA 4-2346 or 712 Northwestern Bank Bldg.; St. Paul, 55102.

WHITE BEAR LAKE, MINNESOTA: A suburban community of 35,000 and growing fast. Have available several ground floor air-conditioned suites in fireproof building in central business district, free municipal parking lot at second entrance in rear. See N. R. Dittberner, 316 Washington Avenue, White Bear Lake. Telephone Collect any time — 429/7787.

PRACTICE FOR SALE: California, San Diego County. General practice. Five-year average gross over $60,000. Modern office for lease. Full equipment included in the sale. No cash necessary. Open district hospital. Write: MINNESOTA MEDICINE — 302; 496 Lowry Medical Arts Building, St. Paul, 55102.

The Blue Shield

New Minneapolis Director

Dr. Charles A. Neumeister, a Minneapolis physician, has been elected to the board of directors of Blue Shield. He replaces Dr. C. A. McKinlay, who resigned for reasons of health.

Dr. Neumeister is a member of the House of Delegates of the American Medical Association, fellow of the American College of Surgeons and fellow of the American Proctologic Society.

Dr. McKinlay was honored by the Blue Shield board in a special resolution to express "appreciation and esteem for him as one of the original members of the Board of Directors."

Dr. McKinlay had served Blue Shield since January 4, 1947.

Living Science Library

Blue Shield has provided the Saint Paul Science Museum with a collection of science teaching aids called The Blue Shield Living Science Library.

The Library is designed to aid young students to delve deeper into the biological sciences and encourage them to a career in Medicine.

The Blue Shield collection consists of more than 30 science teaching aids and models ranging from microscopes to life-size, take-apart models of the human anatomy. The equipment is now being used by the Science Museum in its formal teaching program for bright young science students.

The guest speaker for the opening session was Joseph Mayo, managing curator of the Duluth Zoo and grandson of the founders of the Mayo Clinic.

New 'Senior Citizen' Plan

Blue Shield's new Senior Citizen program, introduced last fall, is continuing to attract subscribers. The coverage is available to persons age 65 and older and offers the combination of medical-surgical as well as hospital and nursing home coverage.

The hospital portion of the program offers 90 days of care per year for each separate illness. The plan has no dollar limit on the cost of hospital "extras," but to hold down premium costs, the payment is on an 80/20 basis. Two options are offered for hospital room costs, either $15 or $10 per day.

The medical-surgical portion of the program is the standard and well-proven Blue Shield Citizen contract. It offers in-hospital medical care benefits for up to 120 days as well as benefits for generally accepted surgical procedures. In addition, the program provides anesthesia coverage as well as outpatient diagnostic laboratory and X-ray benefits.

Today, Blue Shield provides coverage for about 75,000 Minnesota Senior Citizens.

Training Sessions

Blue Shield's "service seminars," designed to help doctors' assistants give better service to subscribers, will continue through 1965.

The seminars focus attention on ways to speed claim processing, tell about various coverages and give special emphasis on new ways to give better service to area residents.

A portion of the program is reserved for questions so that individual attention can be given to any special problems encountered by assistants.

The training sessions, now in their third year, have met with considerable success. The over-all effect is speedier and more complete flow of information from the doctor's office to Blue Shield. In turn, this is rewarded by faster payment of claims, less paperwork, better satisfied patients and Blue Shield subscribers.

Every man is a damn fool for at least five minutes every day; wisdom consists in not exceeding the limit. — Elbert Hubbard

---

Adam was a gardener and God, who made him, sees that half of all good gardening is done upon the knees. — Rudyard Kipling

---

Junk shop near a railroad crossing in Denver carries this sign: "Go Ahead — Take a Chance. We'll Buy the Car."

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*A.M.A. Council on Drugs: J.A.M.A. 183:469 (Feb. 9) 1963.

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DOSAGE: 1 or 2 teaspoonfuls or 1 or 2 tablets 3 times a day before meals. The feeling of warmth and tingling of the skin is a desirable effect. If this reaction is too pronounced reduce dosage.

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REFERENCES:

1. Goodgold, J., Use of Nicotinic Acid-Glycine Mixture in Treatment of Peripheral Vascular Disease, Clinical Medicine 7:12 (1960).
2. Gustafson, Jr. et al. Use of Glycine in the Treatment of Peripheral Vascular Disease, Surgery 25:539 (1949).

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Side Effects: Constipation, dizziness, dysuria, headache, hyperglycemia, hyperuricemia, leukopenia, muscle cramps, nausea, purpura, thrombocytopenia, transient myopia, urticaria, vomiting and weakness.
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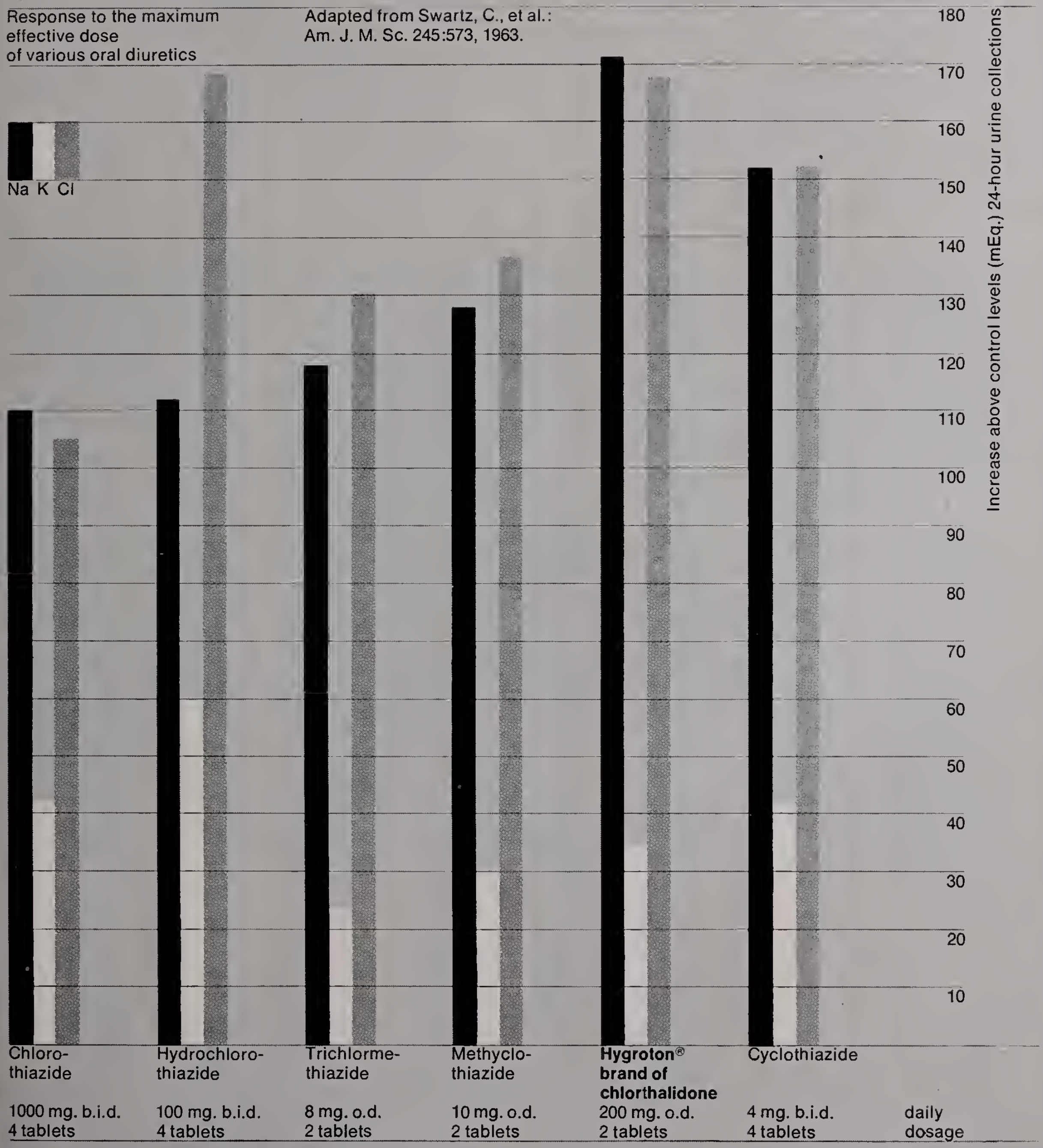

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APRIL 1965

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*Lennox, W. G.: Epilepsy and Related Disorders, Boston, Little, Brown and Company, 1960, vol. 2, p. 865. 432R65

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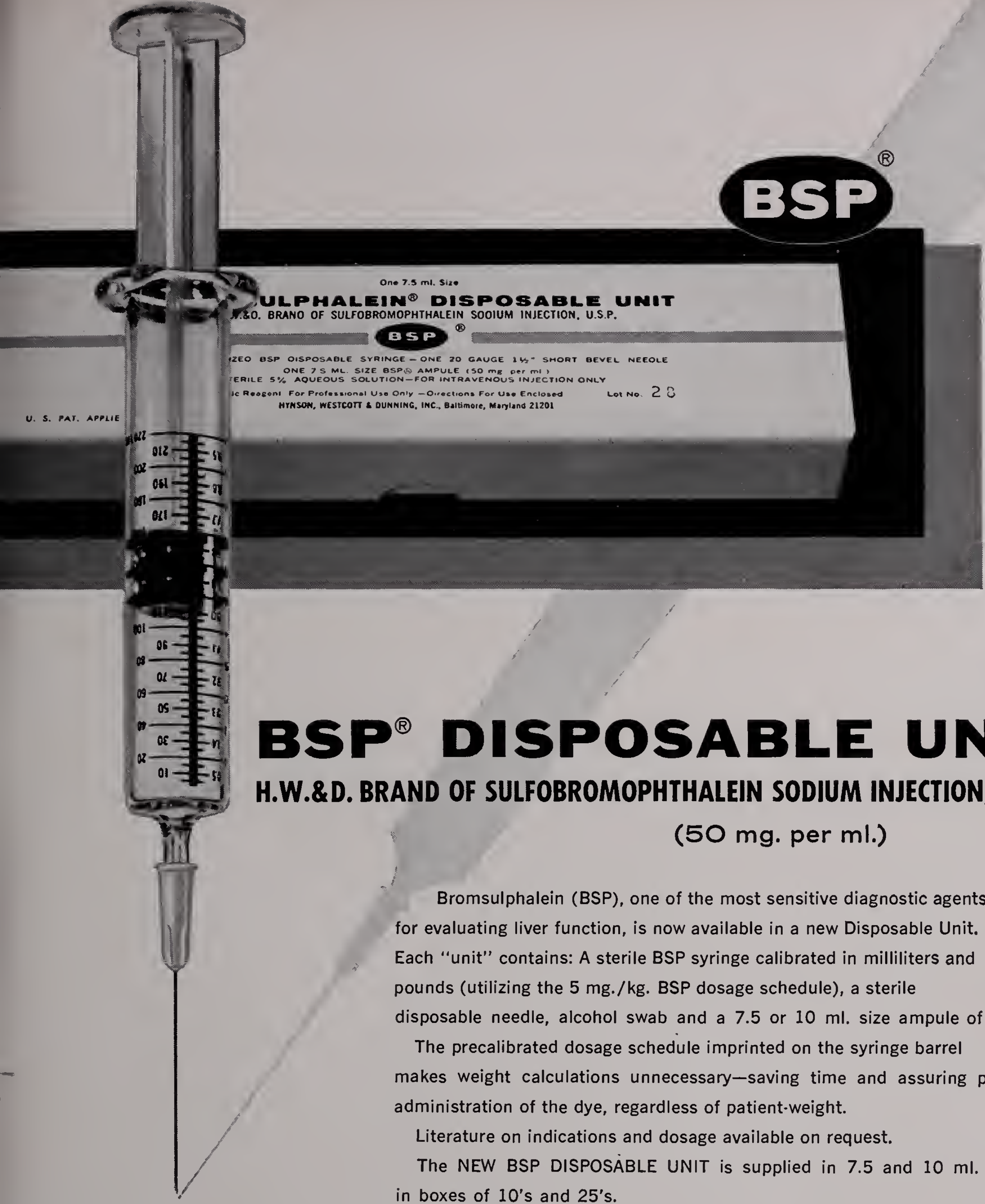
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Bibliographical references should be limited to twelve and should be typed in conformity to the method used by the Index Medicus. They should be numbered consecutively in the order in which they first appear in the text. Book references should give the name of the author, title, edition number, publisher, and the year.

Illustrations (photographs, tables, and graphs) should be submitted on separate sheets of paper and not combined in the text. Instructions for combining photographs are acceptable.

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An award will be given at the annual meeting to the author of the most meritorious manuscript for the preceding year.

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a working analgesic for the active arthritic

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As with any drug containing prednisone, Arthralgen-PR is contraindicated, or should be administered only with care, to patients with peptic ulcer, tuberculosis, nephritis, diabetes mellitus, acute psychoses, Cushing's syndrome (or Cushing's disease), overwhelming spreading (systemic) infection, or predisposition to thrombophlebitis.

Arthralgen-PR is generally contraindicated in patients with uremia and viral infections, including poliomyelitis, vaccinia, ocular herpes simplex, and fungus infections of the eye. It is also contraindicated in patients with chicken pox or susceptible persons exposed to it.

SUPPLY: Arthralgen (white, scored) and Arthralgen-PR (yellow, scored) tablets are available in bottles of 100 and 500.

REF: 1. Boreus & Sandberg, ACTA. PHYSIOL. SCAND., 28:266, 1953. 2. Cohen, et al.: J.A.M.A., 165:225, 1957.

President's Letter

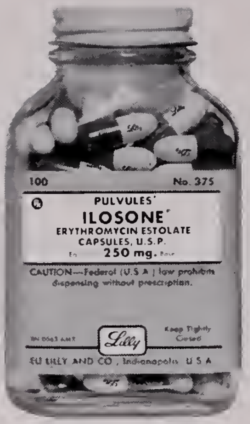
At a special meeting in February, the House of Delegates of the American Medical Association voted to support the Herlong-Curtis bill (HR 3727), which would encourage the use of voluntary health insurance and prepayment plans in the implementation of Kerr-Mills programs for persons more than 65 years old. This bill, which the AMA has called "Eldercare," would permit a state to have a health-oriented agency supervise or adminster the program which provides for a wide spectrum of medical care in which a citizen more than 65 years of age would pay all, part or none of the cost, depending on his income. An income-information statement serving as the sole eligibility test of need is proposed. I suggest that you study the more detailed explanations of this bill so that you may support it in a knowledgeable way. At the special meeting the delegates also asked the Board of Trustees to study the "desirability and feasibility of extending the principle of federal and state aid under the Kerr-Mills principle to persons below the age of 65 who need help." They also urged that the professional services of pathologists, radiologists, physiatrists, and anesthesiologists be excluded from any bill which excludes other physicians' services. In whatever way hospital services may be provided, the methods suggested in Eldercare for the payment of physicians' services are sound.

In the past few years, many resolutions which concern the economic aspects of medical care have been introduced in the AMA House of Delegates. At the present time, specialist societies, particularly those associated with the American Society of Internal Medicine, are preparing plans to be discussed. Many physicians are asking that organized medicine give more attention to planning for an adequate method of protection against catastrophic expense in medical care. One theme in common with Eldercare which runs through most of the proposals is the use of voluntary private insurance and prepayment plans. With the AMA leading the way, physicians will place great emphasis on this mechanism in their thinking for the future, and it is obvious that interest and cooperation of the insurance industry and the Blue Shield and Blue Cross plans will be necessary. It is reported that Blue Shield has shown the greatest interest in the latest proposals. We recall that nearly 30 years ago, it was the Doctors' Plan, Blue Shield, which led the way in helping physicians accomplish their goal of protection against medical costs of the low income group. Perhaps Blue Shield will again be a leader, which emphasizes that at both national and states levels there must be the closest cooperation between medical societies and the Blue Shield organization so that Blue Shield will be, in fact, the Doctors' Plan. It is my hope that the report of the Minnesota House of Delegates ad hoc committee to study Minnesota Blue Shield will have acceptable suggestions for cementing closer liaison between our medical association and Minnesota Blue Shield.

J M Stickney M.D.

J. M. Stickney, M.D.
President
Minnesota State Medical Association

An added margin to meet an extra challenge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Contraindications: Ilosone is contraindicated in patients with a known history of sensitivity to this drug and in those with preexisting liver disease or dysfunction.

Side-Effects: Even though Ilosone is the most active oral form of erythromycin, the incidence of side-effects is low. Infrequent cases of drug idiosyncrasy, manifested by a form of intrahepatic cholestatic jaundice, have been reported. There have been no known fatal or definite residual effects. Gastro-intestinal disturbances not associated with hepatic effects are observed in a small proportion of patients as a result of a local stimulating action of Ilosone on the alimentary tract. Although allergic manifestations are uncommon with the use of erythromycin, there have been occasional reports of urticaria, skin eruptions, and, on rare occasions, anaphylaxis.

Dosage: *Children under 25 pounds*—5 mg. per pound of body weight every six hours. *Children 25 to 50 pounds*—125 mg. every six hours. *Adults and children over 50 pounds*—250 mg. every six hours. For severe infections, these dosages may be doubled.

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Orthostatic Hypotension*

S. SCOTT NICHOLAS, M.D.**
Minneapolis, Minnesota

IN 1925 Bradbury and Eggleston[1] described postural hypotension as a syndrome; patients so affected experienced a fall in blood pressure to hypotensive levels whenever they assumed the upright position. The original report included three cases; subsequently many more cases have been reported and the condition is well documented.[2] The syndrome, orthostatic hypotension, is manifested by the following:

1. The heart rate remains fixed when the patient assumes the upright position (noted in about 50% of instances); 2. Various degrees of anhidrosis (occurs in about 33%); 3. A low basal metabolic rate; 4. An elevated blood urea level; 5. Slight and variable signs of central nervous system disease; 6. Nocturnal polyuria; 7. Occasionally anemia.

The anhidrosis is said to begin as a stocking-and-glove type of distribution and may eventually involve the whole body, usually sparing the face. The neurologic deficits that may be observed include increased deep tendon reflexes, reduced ability to perform alternating motion of the hands and feet, mask-like facies, tremor, muscular rigidity suggestive of Parkinsonism and positive Babinski reflexes. In some patients slurring of the speech and a decrease in intellectual faculties are noted.

Etiologic Factors

Among the various pathological processes that can cause orthostatic hypotension are Addison's disease, central neuropathic conditions (e.g., syringomyelia, tabes, Parkinsonism, etc.), and autonomic neuropathies. These must be considered in the differential diagnosis and be excluded by appropriate studies; circulatory disturbances induced by hypovolemia or by hypokalemia must likewise be excluded. Idiopathic orthostatic hypotension is probably an autonomic neuropathy.[2] Most of the evidence now available incriminates the neuroeffector junction of the sympathetic nerve fibers in the vascular bed.[3,4] It is felt that there is a failure of release of norepinephrine at this level, and there is clinical evidence to suggest that the parasympathetic component may also be involved.[4] For example, massage over the carotid artery fails to lower the arterial pressure and elevate the pulse rate in some patients. In others a lack of response of gastric secretion to insulin-induced hypoglycemia has been observed. It is felt that these findings indicate defective parasympathetic system function.

Treatment

The approach to the treatment of orthostatic hypotension has followed three main lines: mechanical devices, vasoconstrictive agents and extracellular fluid expanders. The first involves the use of such devices as abdominal support, elastic stockings and even pressure suits. Secondly, various vasoconstrictors or pressor drugs such as ephedrine and vasopressin have been employed, the latter given as the tannate in oil or by nasal inhalation of the whole posterior pituitary extract.

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Extracellular Fluid Expanders

Gregory[5] was the first to employ a drug designed to expand the extracellular fluid balance in a patient with idiopathic orthostatic postural hypotension. In 1945, he reported on the effective use of desoxycorticosterone. The treatment was successful, but the method of administration was somewhat cumbersome because injections of desoxycorticosterone suspended in oil were required three times a week. Because of the similarity of its action to desoxycorticosterone, 9 alpha-fluoro-hydrocortisone was suggested for the treatment of postural hypotension due to autonomic dysfunction.[6] This substance is a potent salt-retaining mineral corticoid with weak antiphlogistic activity. It can be administered orally. In 1959, two cases successfully treated with low doses of this preparation were reported.[6] Wagner,[2] in his 1959 review, cited the case of a 21-year-old patient, severely incapacitated by the disease, who had been treated successfully with this preparation for the preceding three years. In 1962, Schrager et al. reported the use of this preparation in six patients.[7] The symptoms caused by the hypotension were successfully controlled in all but one patient. The neurological symptoms that are occasionally seen with this syndrome are not helped by 9 alpha-fluoro-hydrocortisone.

Case Report

A 73-year-old white male first presented to this hospital on July 3, 1962. He had experienced episodes of weakness and dizziness during the preceding five years; these had become much worse in the previous two weeks. He had become almost totally incapacitated by the dizziness which manifested itself primarily in the morning. Upon arising from the supine or sitting position, he would become extremely "lightheaded" and on several occasions fell. However, he never totally lost consciousness. The symptoms tended to abate toward the late afternoon. The patient's wife had noted that his hearing acuity had decreased and that he could hear words but often could not interpret them (receptive aphasia.)

The patient had been evaluated at another hospital where the diagnosis of postural hypotension was confirmed. Conventional therapeutic attempts failed and the patient was referred to Hennepin County General Hospital.

Physical Examination

Physical examination revealed an elderly, healthy-appearing white male. His blood pressure and pulses were as follows: supine: 140/90 — pulse 90/min.; sitting: 90/60 — pulse 100/min.; standing: 50/30 — pulse 110/min. He was oriented in all spheres but was noted to have very slow mentation and difficulty in expressing himself. He had a mask-like facies and an intention tremor without other evidence of rigidity. The remainder of the neurological and physical examination was unremarkable.

Laboratory Observations

Laboratory results at this time revealed: hemoglobin, 11.7 gm.% (subsequently 13 gm.% after two months of iron therapy); wbc 7700 (70% PMN's, 27% lymphocytes, 3% monocytes); urinalysis: cloudy, yellow, sp. gr. 1.014, albumin, sugar and cellular elements absent; fasting blood sugar 91 mgm.% per 100 ml.; and blood urea nitrogen, 30 mgm.% per 100 ml. A chest X ray showed no evidence of active disease and an electrocardiogram was normal. A glucose tolerance test revealed levels of 303, 80 and 90 mg. per 100 ml. at one, two and three hours respectively. Electrolytes were as follows: CO_2 combining power, 29 m.Eq/L; clorides, 90 m.Eq/L; sodium, 142 m.Eq/L; potassium, 4.75 m.Eq/L.

Treatment

Treatment for the postural hypotension initially consisted of an abdominal binder, elastic bandages for the legs, and ephedrine by mouth. No improvement was obtained in the next six weeks. Subsequently dexedrine and methyl testosterone were used without benefit. These medications were then discontinued and a trial of 9 alpha-fluoro-hydrocortisone (Florinef®) was undertaken. Beneficial results were almost immediate and striking. The patient again became self-sufficient, able to dress himself, help around the house and go for long walks. His blood pressures after the first four days of therapy were: 108/58 (sitting) and 104/54 (standing). Initially there was a slight fluid retention and diuretics were required. Throughout the period of observation the electrolytes were stable (see Table).

Progress

Six weeks after the commencement of therapy the supine blood pressure was elevated, 160/110; the dose of the steroid was lowered. The adjustments in dosage are indicated in the Table. During the first six months of treatment, the patient complained of morning headaches; these were relieved by salycilates and to some degree by elevating the head of the bed. At first the elevated supine blood pressure caused some concern as did the gradual weight gain. Since the peripheral edema was only moderate, it was felt that much of the weight gain was due to improved food intake rather than to fluid accumulation.

The following regimen was finally established: 0.1 mgm. of Florinef® b.i.d. six days a week, 0.1 mgm. on the other day (Tuesday); 50 mgm. of hydrochlorthiazide one day each week (Friday), and supplemental potassium chloride, 1.0 gm. daily. An antacid was given twice daily. On this regimen the patient's weight remained relatively stable and the blood pressure when supine remained fairly constant at 170/90-100 mm. of mercury. The problem of both postural hypotension and hypertension was minimized. After six months of observation on this regimen the patient returned to the care of his private physician. The latter reported that the patient's mental status had continued to deteriorate but the blood pressure and serum electrolytes remained at comparable levels (Mar. 2, 1964, see Table). It is of interest that the symptoms of hypotension tended to recur, in a mild form, on the day following the administration of the diuretic agent. The patient's neurological symptoms were unaffected by the therapeutic program. Schrager et al.[7] have observed similar trends in their patients.

Discussion

In patients responding favorably to 9 alpha-fluoro-hydrocortisone, the supine blood pressure is moderately elevated over pretreatment levels. The pressure still falls more than would be considered normal when the individual stands or sits; but the drop in pressure is less marked than before treatment and the undesirable symptoms of postural hypotension do not occur.

Date	October 1 1962	October 5 1962	October 29 1962	November 19 1962	December 31 1962	May 14 1963	June 25 1963	August 22 1963	March 2 1964*
Blood Pressure (Sitting)	110/60	108/58	130/80	146/108	146/84	170/90	120/68	146/86	174/96
Weight (Pounds)	179	184	177	132	180	195	189	188	—
Dosage of 9 alpha-fluoro-hydrocortisone	1.0 mgm. b.i.d.	0.5 mgm. daily	0.5 mgm. daily	0.1 mgm. t.i.d.	0.1 mgm. b.i.d.	0.1 mgm. alternating b.i.d. and once daily	0.1 mgm. b.i.d. 6 days per week; 0.1 mgm. on 7th	same	same
Dose of Hydrochlorthiazide						50 mgm. daily	50 mgm. once/week	same	same
Serum Electrolytes:									
CO_2 Combining Power (m.Eq/L)	29	30		26	30	30	33		
Chloride (m.Eq/L)	99	95	102	100	101	98	96		
Sodium (m.Eq/L)	142	142	146	146	150	147	144		145
Potassium (m.Eq/L)	4.75	3.45	4.15	4.9	4.6	3.8	3.9		3.5

*data supplied by private physician

Clinical observations in a patient exhibiting orthostatic hypotension.

Florinef® (9 alpha-fluoro-hydrocortisone) is a potent mineral corticoid. For this reason, it was hypothesized that its therapeutic effect in idiopathic orthostatic hypotension may be due to an expanded intravascular fluid volume.[6,8] It has also been suggested[6] that the sodium retention induced by this corticoid stimulated the posterior pituitary to secrete increased amounts of vasopressin. However, Schrager et al.[7] showed that there was no *sustained* change in serum electrolytes, body space measurements, or exchangeable sodium or potassium. Their studies indicated that an acute expansion of the extracellular fluid with some sodium retention did occur, but on a long-term basis these changes tended to correct themselves. These investigators also measured urinary and plasma corticoid levels in patients under treatment and failed to find evidence for a suppression of adrenal cortical function.

Thus it would appear that the therapeutic effect of 9 alpha-fluoro-hydrocortisone is related in some way to its influence on sodium metabolism, but the exact mechanism involved is not clear.

Summary

A case of idiopathic orthostatic hypotension was effectively treated with 9 alpha-fluoro-hydrocortisone.

The mechanism by which 9 alpha-fluoro-hydrocortisone exerts a favorable effect is as yet not satisfactorily explained.

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Pliny's Treatment of Ulcers of the Head

"Running ulcers of the head are successfully treated with salt and applied.

The fat, too, of the fox is highly spoken of, but greatest value is set upon cats' dung applied in a similar manner with mustard. Bull's urine, or stale human urine, in combination with cyclaminos** and sulphur has likewise been used; but the most effectual remedy is calf's gall, a substance which, when heated with vinegar, has also the effect of exterminating lice."

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*See Minnesota Medicine June, 1964, Page 716.

**Cyclamin — a hemolytic agent, also an emetic and purgative.

You can usually identify a smart man by his looks. — C.O.R.

The Use of Total Starvation in the Management of Chronic Obesity*

ALVIN L. SCHULTZ, M.D.**
LAURA A. WERNER, B.S.
AARON KERLOW, M.D.†
Minneapolis, Minnesota

PERIODS OF total starvation have been suggested in the treatment of chronic intractable obesity.[1,2] Obese patients have been totally fasted for as long as 117 days without serious side effects.[3] It is now apparent that the obese person who does not respond to hypocaloric diets will consistently lose weight when placed on total caloric deprivation. The present investigation was undertaken to determine the effect of starvation on adrenal cortical function.[4] However, observations were also made on the general effects of starvation in obese subjects, and these results are reported here.

Materials and Methods

Material

Seventeen obese human subjects were obtained as volunteers from among patients attending the Mount Sinai Hospital Outpatient Clinics. Fourteen were women and three were men, ranging in age from 14 to 64 years, and in weight from 188 to 317 lbs. The age, height, ideal and actual weights of each subject are shown in Table 1. None had clinical signs of adrenal cortical hyperfunction, diabetes mellitus, or significant disease other than marked obesity. All had been obese for many years and unable to reduce their weight through hypocaloric diets. Each patient had been receiving sufficient calories to maintain weight stable for at least two weeks prior to inclusion in the study. Each was hospitalized and taken off medications during the period of study.

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*This study was supported by grants from the John A. Hartford Foundation, New York, N. Y., the Minnesota Heart Association, and the General Medical Research Fund of Mount Sinai Hospital.

**Director, Department of Medicine, Mount Sinai Hospital Associate Professor of Medicine, University of Minnesota.

†Chief Medical Resident, Mount Sinai Hospital Medical Fellow, University of Minnesota Graduate School.

Measurements of adrenal cortical function, hemograms, blood urea nitrogen, fasting and post-prandial blood sugars, serum cholesterol, serum uric acid, urinalysis and electrocardiograms were made on each subject. Electroencephalograms were performed on five patients.

After obtaining the base line measurements, twelve obese women were put on total starvation for a period of 13 days. During this period, fluid intake was maintained at 2000 ml. daily in the form of water, tea, coffee, and up to three bottles of a dietary cola drink (three calories per bottle). Activity was limited to bathroom privileges and walking within their hospital rooms. At the end of the 13-day fast period, control measurements were repeated and the patients discharged from the hospital on a 1200 calorie diet.

Methods

The following measurements of adrenal cortical function were made: (1) 24-hour urinary excretion of 17-hydroxycorticosteroids (17-OHCS) and 17-ketosteroids (17-KS), (2) plasma 17-OHCS at 8:00 PM and 8:00 AM, and (3) plasma 17-hydroxycorticosteroids response to adrenocorticotrophic hormone (ACTH) (25u administered intravenously as a four-hour infusion in 500 ml. normal saline).

Plasma and urinary 17-hydroxycorticosteroids were determined by the method of Porter and Silber as modified by Peterson et al.[5] Urinary 17-ketosteroids were measured by the method of Drekter as modified by Klendshoj et al.[6] Serum uric acid was measured by the method of Kern and Stransky as modified by Archibald.[7] Plasma and urine acetone was determined qualitatively by the method of Rothera. Blood-urea nitrogen, blood sugar, and serum cholesterol were measured by standard methods.

Results

Adrenal Function Before Starvation

Measurements of adrenal cortical function in 17 obese subjects while on adequate caloric intake are shown in Table 1. Although the mean values for 8:00 PM and 8:00 AM plasma 17-hydroxycorticosteroids were within the normal range, the morning level was higher than the mean of 13 mcg% established in our laboratory for lean normal subjects. Four patients had definitely elevated values for 8:00 AM plasma 17-hydroxycorticosteroids (above 22 mcg%), and one patient (H. W.) showed no diurnal difference. The mean urinary excretion of 17-hydroxycorticosteroids and 17-ketosteroids,

TABLE I

Adrenal Cortical Function in 17 Obese Subjects While on Adequate Caloric Intake

Subject	Age (Yrs.)	Height (Inches)	Weight (Lbs.)	Ideal Weight	% of Ideal Wt.	Plasma 17 OHCS (mcg.%) 8:00 PM	8:00 AM	After ACTH	Urine (mg./24 hr.) 17 OHCS	17 KS
J. W.*	14	70.5	317	160	198	—	25.6	58.0	10.5	18.3
W. W.*	54	67.0	211	147	144	9.0	13.0	45.0	8.9	11.6
M. S.*	22	71.0	244	165	148	3.4	18.0	65.8	10.6	20.6
F. N.	25	62.0	188	119	158	—	9.8	33.2	3.7	10.6
C. K.	31	66.5	212	135	157	—	18.3	45.0	9.0	10.6
F. Y.	47	62.0	276	119	232	—	17.2	47.4	6.5	10.5
R. M.	31	67.5	263	139	189	5.6	18.6	47.0	13.1	25.7
M. M.	64	64.0	255	126	202	12.0	18.4	44.8	3.6	6.0
A. D.	40	64.0	210	126	167	12.0	26.5	58.0	5.5	7.4
H. W.	50	62.0	192	119	161	18.7	19.1	44.0	9.9	15.3
M. D.	45	66.0	287	146	196	6.6	16.0	39.8	13.5	10.7
E. P.	29	69.0	212	147	144	7.2	29.0	52.9	10.5	6.3
D. M.	54	60.0	278	113	246	6.0	16.4	42.4	10.0	25.8
D. S.	29	67.5	283	139	204	8.7	19.5	49.0	12.7	16.1
F. B.	51	63.5	283	122	232	11.0	19.8	36.4	9.5	7.0
R. S.	19	63.0	244	122	200	10.8	23.4	51.8	7.9	9.9
I. J.	33	64.0	224	126	178	3.5	18.6	—	—	11.9
Mean	38	65.3	246	134	186	8.8	19.2	47.5	9.1	13.2

*Male subject

and the response to ACTH were within normal limits. Two patients had elevated urinary 17-ketosteroid excretion and two had slightly elevated 17-hydroxycorticosteroid excretion.

Weight Loss During Starvation

By the end of the 13-day starvation period, the 12 obese women had lost an average of 23 lbs. per individual (Table 2). The mean weight loss per day of starvation was 1.8 lbs. (range: 1.2-2.7 lbs./day). It is apparent from Figure 1 that the daily weight loss was greater during the first week of starvation than during the second.

Side Effects of Starvation

Most of the patients complained of hunger during the first 24-36 hours of fasting. However, hunger was not a problem in any subject after the second day of starvation, even though other patients in the same room were brought food trays at meal times. The fasting subjects not only had little desire to eat, but also had to be reminded to drink fluids in order to keep their daily intake at 2000 ml. By the fourth starvation day, most of the patients had become listless and apathetic, with little interest in physical or intellectual activity. None were significantly depressed. Some complained of mild headache and all had a decreased number of stools during the starvation period. At the end of the 13-day fast, most of the patients had to be urged to resume eating, and several asked to continue on starvation for a second two-week period. There were no significant emotional disturbances or other serious side effects during or following starvation.

Biochemical Effects of Starvation

The alterations in measurements of adrenal cortical function, associated with star-

TABLE 2
Weight Loss During 13-Day Period of Total Starvation in 12 Obese Female Subjects

Subject	Age (Yrs.)	Height (Inches)	Wt. Before Fast (Lbs.)	% of Ideal Wt.*	Wt. After Fast (Lbs.)	Wt. Lost (Lbs.)	Daily Wt. Loss (Lbs.)
R. M.	31	67.5	263	189	238	25	1.9
M. M.	64	64.0	255	202	228	27	2.1
A. D.	40	64.0	210	167	193	17	1.3
H. W.	50	62.0	192	161	176	16	1.2
M. D.	45	66.0	287	213	267	20	1.5
E. P.	29	69.0	212	144	193	19	1.5
D. M.	54	60.0	278	246	258	20	1.5
D. S.	29	67.5	283	204	258	25	1.9
F. B.	51	63.5	283	232	262	21	1.6
F. Y.	47	62.0	276	232	241	35	2.7
R. S.	19	63.0	244	200	220	24	1.8
I. J.	33	64.0	224	178	202	22	1.7
Mean	41	64.4	251	197	228	23	1.8

*Ideal weight based on 1959 revised height-weight tables of the Society of Actuaries and the Metropolitan Life Insurance Co. (JAMA 173:1576, 1960).

TABLE 3
Change in Serum Uric Acid During 13-Day Period
Total Starvation In Obese Female Subjects

Subject	Age (Yrs.)	Wt. Before Fast (Lbs.)	Wt. Lost (Lbs.)	Uric Acid Start. (mg.%)	Uric Acid Peak (mg.%)
R. M.	31	263	25	6.0	12.5
D. M.	54	278	20	7.0	16.4
D. S.	29	283	25	9.8	17.2
F. B.	51	283	20	7.0	13.6
R. S.	19	244	24	6.4	13.0
I. J.	33	224	22	4.6	11.1
Mean	36	262	23	6.8	14.0

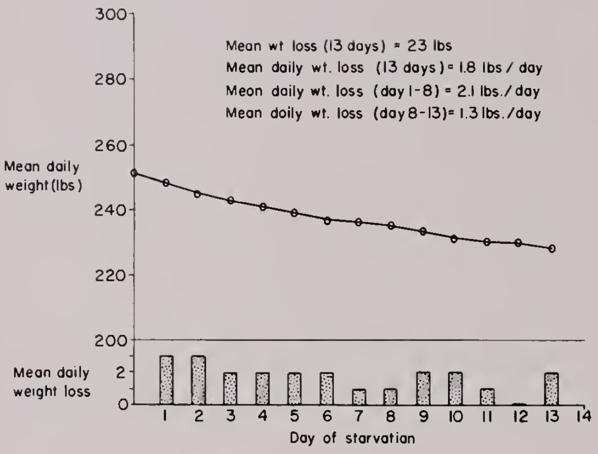

Fig. 1 — Rate of weight loss (mean values) for twelve obese women during a 13-day period of total starvation.

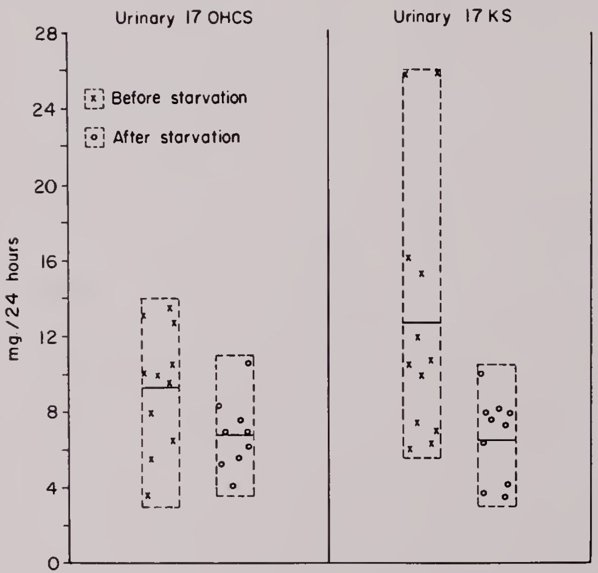

Fig. 2 — The effect of starvation on the 24-hour excretion of 17-hydroxycorticosteroids (17-OHCS) and 17-ketosteroids (17-KS) in the urine. Each x and each o represent a value for a single patient. The horizontal lines indicate the mean values.

vation, have been reported elsewhere[4] and are summarized in Figures 2 and 3. Urinary excretion of 17-hydroxycorticosteroids and 17-ketosteroids was decreased by 27 per cent and 47 per cent respectively. Plasma 17-hydroxycorticosteroids, measured as Porter-Silber chromogens, showed a marked increase during starvation, with a loss of the normal diurnal change. Response to ACTH was also increased. However, measurement of plasma cortisol by a more specific isotope dilution chromatographic technique did not show an increase in plasma cortisol, indicating that the increase in plasma Porter-Silber chromogens was due to nonadrenal steroidal material appearing in the plasma during starvation. The nature of this material was not determined in our studies.

All of the fasting patients showed mild to moderate acetonuria; however, five of the twelve had consistently negative plasma acetone. Quantitative ketone body measurements were not made. There was no significant change in plasma CO_2 content during starvation.

Serum uric acid rose markedly in the six women in whom serial measurements were made (Table 3). In some patients the peak serum uric acid level was reached by the sixth to eighth day of starvation, followed by a decrease in level (Figure 4). There were no clinical signs of gouty arthritis in any of the patients.

Blood urea nitrogen, serum cholesterol and blood sugar showed a moderate decrease during starvation, but the significance of these changes could not be tested because of the small numbers of observations made. In three patients, endogenous renal creatinine clearances were measured and each showed approximately a 50-per cent decrease from normal prestarvation values.

Measurements of hemoglobin, sedimentation rate, serum protein-bound iodine and thyroid I^{131} uptake showed no significant change with starvation. Electrocardiograms and electroencephalograms remained normal during starvation.

Discussion

Studies of obese subjects on adequate caloric intakes have shown that obesity is frequently associated with increased urinary 17-hydroxycorticosteroid excretion and increased cortisol production and disappearance rates.[8-15] The level of plasma 17-hydroxycorticosteroids has been reported to be low by some investigators[11,12] and normal by others.[10,13] Simkin[9] found the urinary excretion of 17-ketosteroids to be increased; however, others[8,10] have reported normal values in obesity. In our obese patients before starvation, mean values for evening and morning plasma 17-hydroxycorticosteroids and 24-hour urinary excretion of 17-hydroxycorticosteroids and 17-ketosteroids were within the accepted normal range. There was considerable variation within the group, with a few individuals having definitely elevated values. Elevated plasma 17-hydroxycorticosteroid levels were not necessarily associated with increased urinary excretion of 17-ketosteroids and 17-hydroxycorticosteroids. None of our subjects had low values for 8:00 AM plasma 17-hydroxycorticosteroids and the mean 8:00 AM level was considerably higher than our normal mean for lean subjects. Only one patient did not show a normal diurnal change in plasma 17-hydroxycorticosteroids. Response to adrenocorticotrophic hormones and SU-4885, and suppression with dexamethasone have been reported to be normal.[8,10,12,13]

Whether obese persons with laboratory evidence suggesting adrenal cortical hyperfunction have mild Cushing's disease has not been established. It has been concluded that obese subjects have a greater than normal conversion of secreted cortisol to urinary Porter-Silber chromogens.[12] Reduction in weight has resulted in return to normal of measurements of adrenal cortical function.[8,13,14,16] It has been demonstrated that urinary excretion rates for 17-hydroxycorticosteroids, and to a lesser degree 17-ketosteroids, are correlated with weight, height, and surface area.[17,18] Szenas and Pattee[11] have suggested that obesity is a continuous mechanical stress resulting in adrenal cortical hyperfunction. None of our obese patients had clinical findings of Cushing's disease either before or during starvation. It appears that in some patients obesity is associated with mild adrenal cortical hyper-

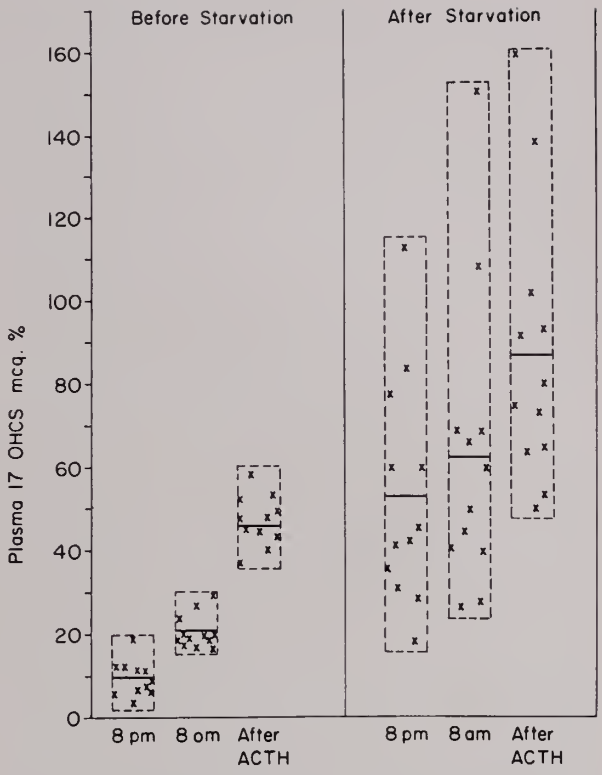

Fig. 3 — The effect of starvation on 8:00 PM and 8:00 AM plasma 17-hydroxycorticosteroid levels (17-OHCS) and response to ACTH. Each x represents a value for a single patient. Horizontal lines indicate mean values.

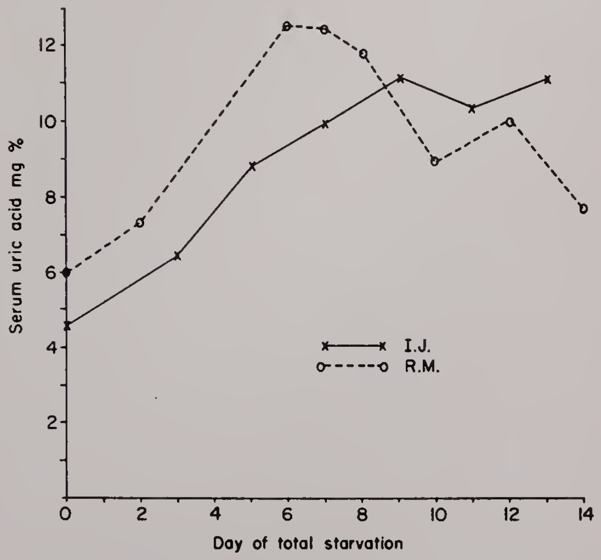

Fig. 4 — Serial values for serum uric acid during starvation in two obese women.

function; however, the increased adrenal cortical activity cannot be implicated as a cause of the obesity.

It has been demonstrated that short periods of total starvation are associated with few side effects, an absence of hunger and a consistent and progressive loss of weight.[1-3] Bloom[1] and Duncan and associates[2] reported an average daily weight loss of 2.5 to 3.0 lbs. Drenick et al.[3] observed patients during more prolonged fasts up to 117 days and reported a mean daily weight loss of less than 1 lb. Our patients lost an average of 2.1 lbs. per day during the first week but only 1.3 lbs. per day during the second week. This suggests that there is an initial excessive loss of body water, perhaps through both renal and insensible pathways, which decreases with continued fasting. We have also observed a rapid gain of 5-7 lbs. in weight during the first week post-starvation, not accounted for by caloric intake, which may represent retention of fluid and rehydration. None of our patients showed clinical signs of dehydration. With very prolonged periods of total starvation, orthostatic hypotension and marked losses of body protein and potassium have been reported.[3]

Starvation has been found to be almost invariably associated with a marked rise in serum uric acid.[1-3] This was also our observation. Drenick et al.[3] reported attacks of clinical gouty arthritis in two of their eleven patients. Murphy and Shipman[19] concluded that decreased urinary excretion of uric acid was related to a reduction in glomerular filtration rate during starvation, resulting in an alteration of renal tubular transport of uric acid. Cristofori and Duncan[20] have suggested that decreased levels of amino acids and carbohydrates in starving subjects result in diminished competition with uric acid for proximal renal tubular reabsorption, with a subsequent increase in serum uric acid. They found that Probenecid decreased serum uric acid and increased renal excretion of uric acid during starvation. Starvation of eight obese patients with a history of gouty arthritis, produced no acute attacks of gout despite increased serum uric acid levels. These investigators do not consider a history of gout to be a contraindication to periods of starvation up to 14 days.

Our observation of increased plasma Porter-Silber chromogens during starvation is at present not explained; however, it can be concluded that plasma cortisol is not significantly increased during starvation and that fasting for periods up to 14 days does not result in a stress stimulus to either the adrenal or pituitary glands.[7] The decreased urinary excretion of 17-hydroxycorticosteroids and 17-ketosteroids may be related to diminished renal excretory ability during starvation or decrease in pituitary or adrenal cortical activity.

It can be concluded that even the intractably obese person who does not lose weight on hypocaloric diets, will consistently lose 1-3 lbs. per day on total caloric deprivation. Total starvation for periods of 14-21 days appears to be safe and well tolerated, and there are no apparent, absolute contraindications. Although the obese patient had been restricted in physical activity during starvation, this is probably not necessary. Starvation of the ambulatory patient under close medical observation for short periods would seem to be safe and certainly economically more feasible than hospitalized fasts. The temptation to eat will, however, be greater and his control more difficult. It appears that even very limited food intake reduces the appetite suppression produced by total starvation.

The problem of the long-term management of obesity is not changed by intermittent periods of starvation. The obese patient must still alter his eating habits and attitudes toward food, if he is to continue to keep his weight within reasonable limits. The emotional and psychiatric aspects of obesity are not eliminated by starvation, and may in some cases be aggravated by total fasting. Periods of starvation in the management of obesity probably have their greatest value in demonstrating to the obese patient that he can lose weight, and in resolving the rationalization of many obese persons to the effect that diet and calories are not really involved in their weight problem.

Summary

Studies of adrenal cortical function in seventeen obese subjects on adequate caloric intakes indicated that their mean level of plasma 17-hydroxycorticosteroids was higher than that of normal lean persons. Adrenal cortical function was otherwise normal except for one patient who showed no diurnal change in plasma 17-hydroxycorticosteroids, and three who had moderate elevation of urinary 17-ketosteroid and/or 17-hydroxycorticosteroid excretion.

Total starvation of twelve obese women for a period of 13 days produced a consistent and progressive decrease in weight (mean loss: 1.8 lbs. per day). Serum uric acid and plasma Porter-Silber chromogens rose markedly, and excretion of 17-ketosteroids and 17-hydroxycorticosteroids decreased during starvation. Appetite was decreased and no serious clinical side effects were observed.

It is concluded that short periods of total starvation are a safe and effective way to initiate or supplement a broader program for the management of the obese patient.

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ACHARD-THIERS SYNDROME

(Cushing's Syndrome)

This syndrome first was described in 1921 and is characterized by adenoma or hyperplasia of the adrenal cortex, diabetes mellitus and facial hirsutism in women with a masculine type of hypertrichosis of the face, voice changes, hypertrophy of the clitoris and occasionally a male psychogenic outlook. Obesity of the trunk, stria, acne, hypertension and occasionally osteoporosis may be present. Carbohydrate tolerance is decreased. The syndrome is thought to be the result of overproduction of the various adrenocortical hormones.

Robert H. Durham

It is a property of human nature soon to relax when not impelled by personal advantage or disadvantage. — Wolfgang Von Goethe

The Urea Wash-Out Test*

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NUMEROUS SCREENING procedures for curable renovascular hypertension have been developed. The radioactive renogram,[1] the aortogram,[2] the "Howard test" and its various modifications,[3-5] and a variety of modifications of the intravenous pyelogram[6] are the more common examinations which have been employed. Split renal function studies have enjoyed the best results in predicting the curable disease states. They are, however, time-consuming, require special skills, and are not without morbidity and failure. The examination that the practicing physician resorts to for screening purposes because of its availability and ease of performance is the intravenous pyelogram. But numerous studies have demonstrated the inefficiency of the standard IVP in screening for curable renovascular hypertension.[6] Modifications of this procedure[6,7] have increased its efficiency; but there remains a group of undetectable lesions that represent 10 to 15 per cent of the curable cases.

Applying the basic principles of the renal physiologist, one of us introduced a modification of the intravenous pyelogram,[8] which has been employed in the evaluation of over 500 cases to date at some of the University Hospitals.[9] A review of the results of this examination in the first 407 patients, along with a number of concurrent renograms and aortograms, is the purpose of this paper.

Physiology

For the purpose of understanding what is visualized on the pyelogram the underlying physiological alterations can be oversimplified to two fundamental abnormalities. (1) There is a decrease in bloodflow to intact renal parenchyma, and (2), partially as a result of the first abnormality, hyperconcentration of certain substances excreted by the kidneys occurs. This is accomplished by the relative increase in absorption of sodium, and along with this water in the proximal tubules.

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*Wash-out and flush test used interchangeably throughout this article.

Read before the Minnesota Radiological Society Meeting, February 29, 1964, Minneapolis, Minnesota.

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Detection of Curable Renovascular Hypertension

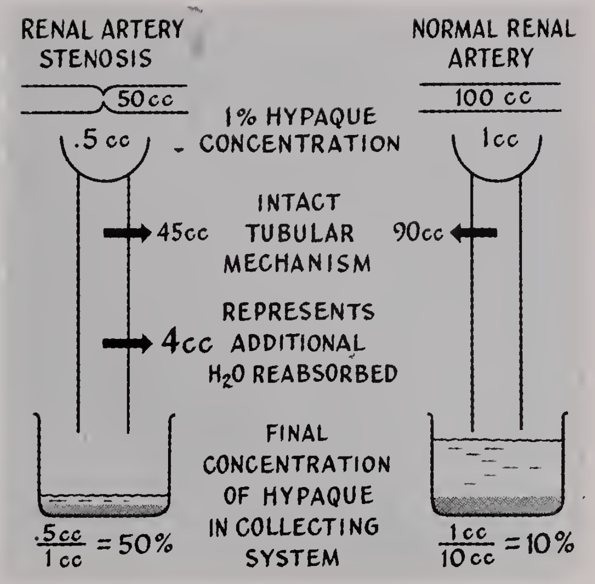

Fig. 1 — Schematic presentation of fundamental physiological abnormality in curable renovascular hypertension as it applies to intravenous pyelography.

The theories for the actual mechanisms by which these disturbances produce an increase in blood pressure are beyond the scope of this paper. Stamey has demonstrated that urea, when infused into the patient undergoing split renal function studies in the dehydrated state, will enhance the hyperconcentration of inulin, para-aminohippuric acid, and related substances.[4]

Hyperconcentration

Whether it be in the radioactive renogram, the routine or fast intravenous pyelogram, the Howard test, or aortography, the fundamental favorable prognostic sign known today is hyperconcentration. Figure 1 is an attempt at a more graphical representation of these physiological alterations. Through the stenotic renal vessel on the right side pass 50 c.c. of blood which is eventually filtered by the intact glomerulus. On the normal side during the same relative time, 100 c.c. have passed. The concentration crossing the glomeruli is equal and approximately one per cent when using 50 c.c. of sodium diatrizoate in an average individual. Also, the concentration of sodium diatrizoate is equal in the ultrafiltrate bilaterally.

Reabsorption

The intact tubular mechanism conserves sodium to the extent that 90 per cent of the water is reabsorbed from the urine on either side. Any substance which is not reabsorbed along with the sodium and water (such as sodium diatrizoate) will be further concentrated in the urine. As first described by Howard, in renal artery stenosis there is in addition an excess reabsorption of water in the tubules on the involved side. This is represented by the 4 c.c. For emphasis the water reabsorbed in the tubules on the abnormal side has been separated into 45 and 4 c.c. In practice, however, no such distinction can be made. In the containers at the bottom of the diagram the original 1 c.c. of hypaque is now 10 per cent of the final volume. On the involved side the original 0.5 c.c. now makes up 50 per cent of the final volume.

In summary, the decrease in glomerular filtration associated with renal artery stenosis is not accompanied by a decrease in tubular reabsorption. If tubular reabsorption were decreased to the same extent, then hyperconcentration would not occur. Since the tubular apparatus continues to reasorb sodium and water at a close to normal rate, hyperconcentration of nonreabsorbable substances (i.e. sodium diatrizoate) occurs.

The increased absorption of water has presumably resulted from the decreased flow of urine down the tubular system, a result of the decreased amount of blood presented to this kidney. Urea has been shown by Stamey to enhance this hyperconcentrating effect, presumably by presenting a large volume of fluid during a relatively short time.[4] In addition, urea is freely diffusable across the tubules, thus acting differently than Mannitol, which is not freely diffusable and perhaps less desirable.

Technique

Table 1 demonstrates the chronological approach to the performance of the urea flush test. The routine intravenous pyelogram preparation and scout film are obtained. No compression is used. Fifty c.c. of 75 per cent sodium diatrizoate are then injected rapidly and intravenously into a Y-tubing, which at one end has 500 c.c. of 8 per cent saline. The routine fast intravenous pyelogram films are taken at 30 seconds, 1, 2, 3, 5, and 10 minutes.

The three-minute film is developed and inspected. If equal concentration in both collecting systems has resulted, then the urea-saline mixture is allowed to run wide open. The 5 and 10-minute films serve as a baseline. Usually the 500 c.c. take from 8 to 10 minutes to infuse. During this infusion five films are obtained, exposed every three minutes.

Contraindications

Contraindications to this test include: (1) an elevated blood urea nitrogen, (2) moderate to severe congestive heart failure, (3) the usual contraindications to the injection of contrast agents.

Approximately 30 to 50 per cent of patients will complain of mild to moderate headache which is transient. Oral water hydration alleviates the majority of symptoms. No serious side effects have resulted.

Case Histories

The following two cases are included to demonstrate the typical findings in renovascular hypertension.

Case 1

A 37-year-old white male had a one-year history of severe hypertension and incapacitating symptoms. Headaches, blurred vision, dizziness, and signs and symptoms of aortic insufficiency were recorded. His blood pressure prior to surgery ranged from 200 to 220 systolic and 130 to 150 diastolic. Figure 2a shows hyperconcentration on the left side at 10 minutes; Figure 2b shows a holdup and positive flush test on the left side; Figure 2c shows the stenotic vessel with poststenotic dilatation. A pressure gradient of 40 mm. of Hq was measured across this vessel at the time of surgery and a bypass graft was performed. Within one week after surgery the blood pressure fell to 150/90. It has remained at this level for one year and the patient has been symptom-free.

Case 2

A 49-year-old white male, with a seven-week history of severe headaches, blurred vision, and dizziness, had preoperative blood pressures of 190 to 200/120 to 130. Figure 3a shows the delayed excretion of contrast in the collecting system on the right side; Figure 3b shows the density of contrast in the right

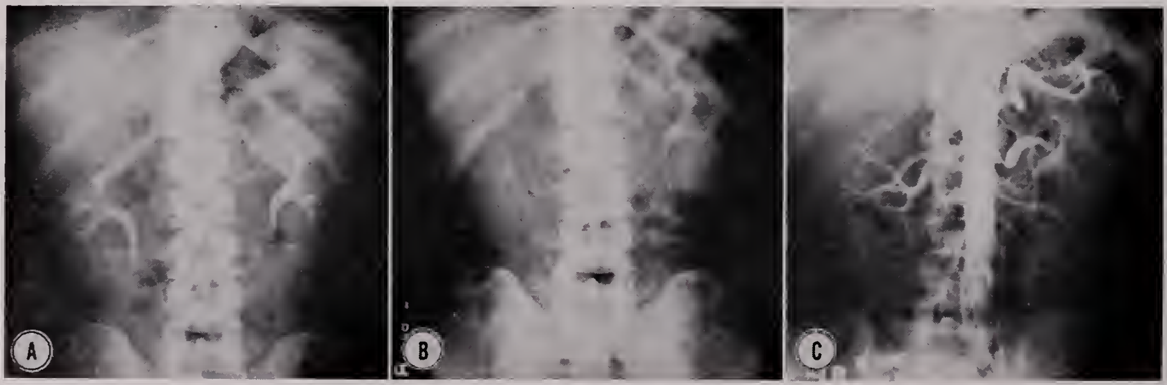

Fig. 2 (a) *Case 1.* Increased density of contrast agent in the left collecting system when compared to right. (b) Under influence of urea diuresis the normal right side washes out and there is a holdup of contrast on the left side. (c) Aortogram demonstrating left main renal artery stenosis with poststenotic dilatation.

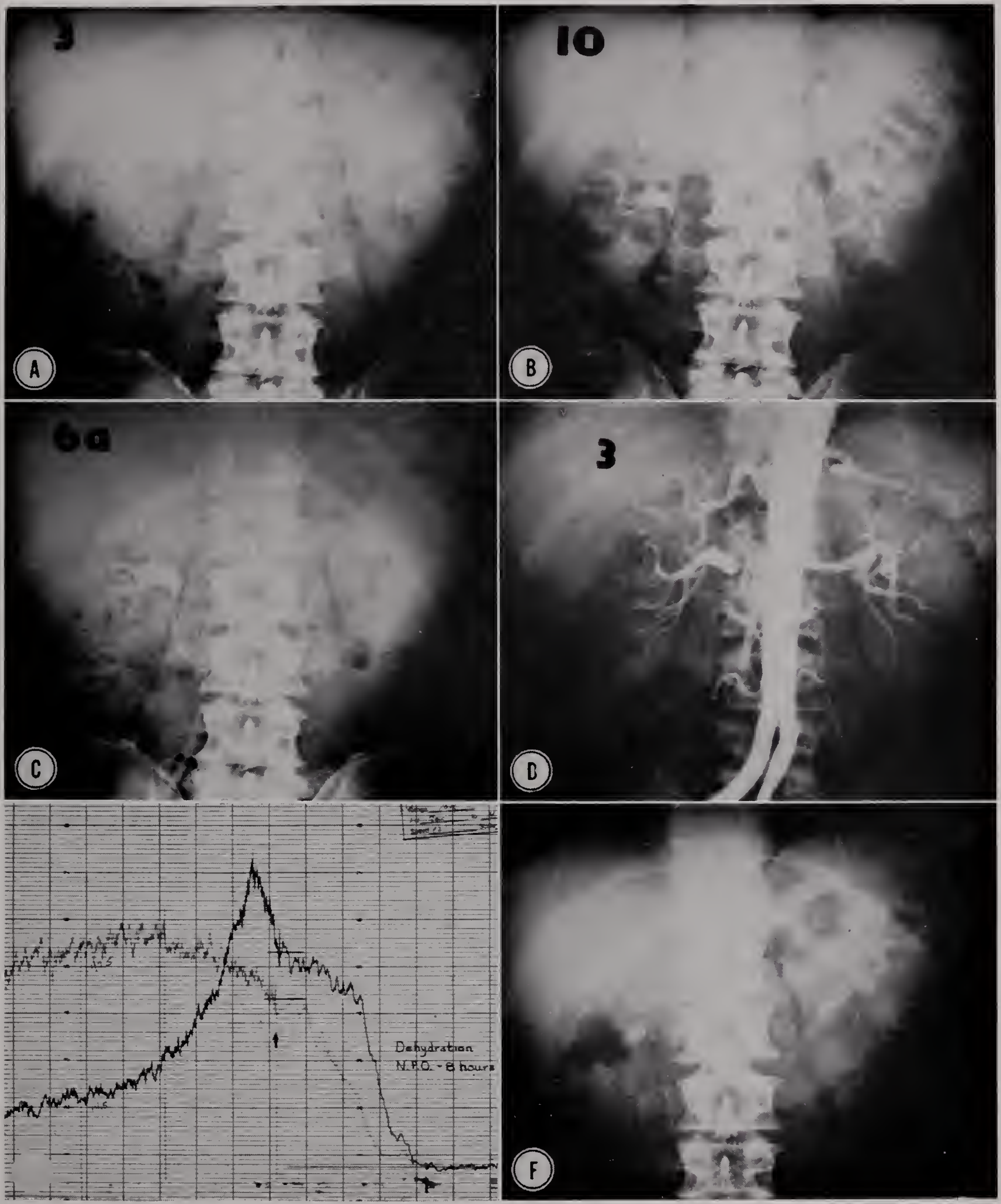

Fig. 3 (a) *Case 2.* Contrast has appeared in the left collecting system at three minutes. (b) At ten minutes there is increased concentration of the contrast agent in the right collecting system. (c) Washing out of contrast from the left collecting system while the right collecting system remains opacified. (d) Aortogram demonstrating right renal artery stenosis with poststenotic dilatation. (e) Renogram with characteristic changes of delayed vascular phase and peak with prolonged excretion on the involved side. (f) Postoperative washout which is equal and normal.

TABLE 1
Procedure — No Compression

1. Scout film.
2. Mix urea with saline (shake vigorously until all dissolved).
3. Start I.V. using Y-tubing with urea saline mixture.
4. Inject 50 c.c. of 75% hypaque as rapidly as possible (usually 20 to 40 seconds).
5. Allow urea to drip slowly to keep open.
6. Take films after hypaque injected at 1, 2, 3, 5, and 10 minutes; check for concentration in pelves (adequate concentration usually on 3-minute film, the 5 and 10-minute films serving as baseline for urea).
7. Allow urea to run wide open after film obtained with adequate concentration (usually 500 c.c. take 10 minutes).
8. Obtain X rays at 3, 6, 9, 12, and 15 minutes after urea starts (label A for After).
9. Check films to be sure study is complete.

TABLE 2
Studies in 407 Unselected Hypertensive Cases

Hospital	No. Cases	Renograms	Aortograms
U. of Minn.	309	126	82
V. A.	64	1	9
Ancker	34	0	5
	407	127	96

TABLE 3
Positive Washouts

Hospital	No. Cases	Normotensive	Improved	No Change
U. of Minn.	9	5	3	1*
V. A.	2	2		
Ancker	1		1**	
	12	7	4	1

*Renal infarct mostly of right kidney, presumably thrombosis of bypass graft.

**Washout remains positive but not as striking. Renal infarct upper pole.

TABLE 4
Aortograms

Hospital	Number	Positive	Surgery	+Washout
U. of Minn.	82	14	11*	9
V. A.	9	2	2	2
Ancker	5	2	1	1
	96	18	14	12

*Two cases operated upon for vascular stenosis without positive washouts. Each had negative split renal function studies and positive renograms. Neither improved postoperatively.

to be greater than in the left on the eight-minute film; Figure 3c shows a positive washout test with holdup of contrast on the right; Figure 3d shows the renogram with the typical pattern for stenosis of the right renal artery; Figure 3e shows the aortogram with stenosis of the main renal artery and poststenotic dilatation; Figure 3f shows the postoperative urea flush test which has equal washout bilaterally.

The patient went to surgery and a vein graft was inserted over the area from which the atherosclerotic plaque was removed. His blood pressure fell immediately to 140/80. Two months later it was recorded as 146/90. He is now completely free of symptoms.

Results

Four hundred and seven unselected hypertensive patients were screened at the University of Minnesota, at the Veterans Administration Hospital in Minneapolis, and at Ancker Hospital in St. Paul over the past year. The examinations performed in these patients are seen in Table 2.

Ninety-six underwent retrograde or translumbar aortography, many of the group because of a high clinical suspicion or abnormal renogram. One hundred and twenty-five renograms were performed at the University.

In the 407, twelve positive cases (3 per cent) were obtained. The results of surgery in these cases are shown in Table 3. Seven patients were normotensive; four have shown significant improvement, and in one University case there was a return of blood pressure to the previous elevated levels two months after surgery. A follow-up aortogram revealed extensive infarction of the middle portion of the right kidney. Unfortunately, the patient refused further care. A similar situation, but with a much less extensive infarction, occurred with the Ancker patient. The important point to be gained from these two cases is that the etiology of the failure of cure in renovascular hypertension deserves considerable study.

Significant improvement was judged to be a drop of 20 degrees diastolic pressure to near normal levels along with complete amelioration of symptoms.

The results of the 96 aortograms are seen in Table 4. Eighteen patients were felt to have a significant lesion compatible with renovascular hypertension. Fourteen of this group underwent surgery; the other four either refused surgery or were deemed too great a surgical risk. Twelve of fourteen had positive flush tests; the results have been presented in Table 4. The other two patients had negative 'split renal' function studies and abnormal renograms; neither improved with surgical correction of the stenosis.

Renograms

Renograms were performed on 126 of these patients being evaluated for hypertension (Table 5). Seventy-six had a normal renogram and a normal urea washout test. Eight within a group of 76 also had aortograms performed, three of which were reported to show renal artery stenosis. One of these stenotic sites was felt to be hemodynamically significant. Only one patient of the entire group exhibited a normal renogram but an abnormal urea washout test and aortogram indicative of renal artery stenosis. This renogram was one of our early studies and was performed with the patient fully hydrated rather than partially dehydrated, as is presently done.

Renograms on 50 patients in this series were reported as abnormal. Twenty-two of these were quite typical for stenosis (delay in appearance and mild depression of peak function, and delay in excretion.) Of these, 17 have also had aortograms, all of which confirmed renal artery stenosis. The five remaining patients are presently being scheduled for follow-up aortography. The patterns from the 28 remaining patients were not typical of renal artery stenosis (rather isolated decreased function and/or delayed excretion,) and these patients had normal urea washout tests.

Summary and Conclusions

The urea flush test represents another application of radiological methods for the detection of abnormal physiological mechanisms. It may be premature to state the value of this test, but results today are encouraging. However, many questions remain unanswered. The role of the "normal" kidney which has been subject to high blood pressures for variable periods of time has not been clearly established. For this reason each patient who has undergone surgery for renovascular correction recently has had biopsies of both kidneys. Possibly this will give greater insight into the problem of curable renovascular hypertension.

The urea flush test presumably will suffer the same pitfalls as have the split renal function studies. With additional experience, it is feared that an occasional case of segmental arterial disease and symmetrical bilateral disease will be missed.

The urea flush test in our hands has proven

TABLE 5
Evaluation of Renovascular Hypertension Using Radioisotope Renograms

76 Normal Renograms	
67	Normal Urea Washout
5	Normal Urea Washout Normal Aortogram
4	Normal Urea Washout Abnormal Aortogram (One hemodynamically significant)
76	

51 Abnormal Renograms

Atypical for Stenosis		Stenosis Pattern	
28	Normal Urea Washout No Aortogram	8	Abnormal Urea Washout Abnormal Aortogram
1	No Urea Washout Abnormal Aortogram	7	Normal Urea Washout Abnormal Aortogram (3 hemodynamically significant)
1	Abnormal Urea Washout Abnormal Aortogram	1	Abnormal Urea Washout Aortogram to be scheduled
		5	Normal Urea Washout Aortogram to be scheduled
30		21	

to be the most reliable prognosticator of curable renovascular hypertension. A larger experience will be necessary before any conclusion can be reached as to its reliability in screening for renovascular hypertension. Therefore, aortography should be performed in all patients in whom there is a marked clinical suspicion of this disease.

Of 407 flush tests 12 were positive. These all showed surgically correctable lesions as evaluated by angiography. Eleven of twelve cases were either cured or significantly improved. One had a surgical failure.

Acknowledgement

The authors extend appreciation to Dr. Donald H. Peterson, Chief of Radiology, Ancker Hospital, for allowing inclusion of data from Ancker Hospital studies.

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WHAT'S YOUR DIAGNOSIS?

The patient was an eighteen-year-old, unmarried girl with onset of illness approximately three months prior to her admission to the hospital. She had lost approximately twenty-five pounds. There had been no nausea or vomiting though she had noted intermittent episodes of gassy eruptions and hyperacidity which was relieved with milk. Bowel function was normal. There had been no evidence of melena. The menstrual period had been delayed ten days and was associated with heavy flow and clots, but in the past two months the menstrual periods had been normal. She was admitted to a hospital, having felt faint and dizzy for three days. She felt no pain.

The physical examination revealed the patient to be pale. Blood pressure was 146/78, pulse 76. The abdomen was soft. Rectal examination was negative, and no mass or tenderness was elicited in the pelvis by digital examination.

Hemoglobin was found to be 6.9 grams, red cell count 2,130,000. Leukocytes and differentials were normal.

After five units of whole blood, the hemoglobin was found to be 14.5 grams, hematocrit 44 volume.

Fluid from the peritoneal cavity revealed an abundance of xanthochromic type fluid.

Numerous other laboratory and X-ray studies were made, all of which were reported to be negative. An operation was done and the diagnosis definitely established.

What's Your Diagnosis? Turn to page 462.

One man with courage makes a majority. — Andrew Jackson

The Effectiveness of Erythromycin in Office Practice

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SHERMAN B. CHILD, M.D.
JOHN A. HIATT, M.D.
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ERYTHROMYCIN IS a wide-spectrum antibiotic of proved effectiveness and unparalleled safety.[1-10] Side effects, including allergic manifestations, have been infrequent and relatively minor. The stearate and ethyl succinate salts have not been known to cause liver dysfunction, as seen with the propionyl ester lauryl sulfate.[11] It is the purpose of this study to examine the efficacy of erythromycin in the treatment of various infectious diseases encountered in an urban clinic devoted to the general practice of medicine and surgery.

Methods

Patients

A total of 159 patients were included in the study. Persons whose conditions were felt to specifically indicate a different antibiotic were excluded. Age distribution of the patients is shown in Table 1.

TABLE I
Age Distribution of Patients Under Study

Age in Years	No. of Patients
Less than 1	4
1-5	26
6-15	29
16-64	92
65 and over	8
	159, total

Diagnoses

Clinical diagnoses, 170 in all, are listed in Table 2. Generally, only the primary diagnosis was recorded when multiple diagnoses were made. However, all cases of acute bronchitis, tonsillitis, sinusitis, otitis media or pneumonia were recorded (these included 11 patients with concurrent diagnoses).

Treatment

Oral preparations (erythromycin stearate tablets and erythromycin ethyl succinate granules for oral suspension*) were administered for varying periods of therapy. Adults and older children received 1 gm. per day while smaller children received 20-30 mg./kg./day; medication was given in four divided doses daily.

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*Supplied by Abbott Laboratories, North Chicago, Illinois, as Erythrocin Filmtab Tablets and Erythrocin Granules for Oral Suspension.

Results

Criteria for a satisfactory result in this study were: (1) complete clinical cure within the period of antibiotic therapy, (2) no subsequent recurrence attributable to the original infection, and (3) no complaint of side effects. According to these criteria, satisfactory results were obtained in 127 patients (see Table 2).

An analysis of the 32 patients recorded as failures revealed that 19 were so classified because they failed to show an adequate clinical response. Sixteen of these were promptly cured with other antibiotics; diagnoses in the other three patients were tonsillitis (probably of viral etiology), acne vulgaris and bronchiectasis. Three patients were recorded as failures because recurrences were reported. The other 10 treatment failures were so classified because of reported side effects including upset stomach, indigestion, and one case each of dizziness and diarrhea. Seven of the 10 patients stopped medication without consulting with their physicians. The complaints of six persons, including those reporting diarrhea and dizziness, were questionable; for example, one of the patients reporting "side effects" was suffering from fever and malaise due to infectious mononucleosis and, in addition, was taking large quantities of aspirin and a cold preparation containing codeine.

Throat cultures, obtained from 22 patients with respiratory infections, and a skin culture from another patient were streaked on-

TABLE 2
The Response of 159 Patients to Treatment with Erythromycin According to Clinical Diagnosis

Diagnosis	No.	Treatment Failures Due to Inadequate Response	Treatment Failures Due to Side Effects	Treatment Failures Due to Recurrent Infection
Bronchitis, acute	53	10	4	
Tonsillitis	25	1	2	2
Sinusitis	25	1		1
Otitis media	13	2		
Pharyngitis	15	1	1	
Upper respiratory infection	10	1	1	
Cellulitis	5			
Adenitis	2			
Cystitis	2			
Pneumonia	2	1		
Acne vulgaris	1	1		
Adenitis, mesenteric	1			
Asthma	1			
Bronchiectasis	1		1	
Felon	1			
Fever, unknown cause	1			
Furuncle	1			
Impetigo	1			
Infectious mononucleosis	1		1	
Laryngitis	1			
Measles, prodromal	1			
Pleuritis	1			
Pustules, cutaneous	1	1		
Salpingitis	1			
Thrombophlebitis, superficial	1			
Tracheitis	1			
Upper respiratory infection, viral	1			
Urethritis	1			
Total	170	19	10	3

to sheep's blood-agar plates. Of these, three yielded beta hemolytic streptococci (all patients responded to treatment); nine yielded Staphylococcus aureus (five patients responded to treatment); four, including the skin culture, grew gram-negative rods (none of the patients responded); and only nonpathogens were found in seven cultures (four patients responded to treatment).

Discussion

Of 32 patients classified as treatment failures, there were nine in whom this classification was questionable. Three of these patients, recorded as failures because of inadequate clinical response, were not cured with other antibiotics; the "side effects" of six patients were considered likely to be due to factors other than the medication under study. Thus, excluding the nine questionable failures, only 16 patients (10%) failed to respond to treatment because the medication lacked adequate antibacterial activity, three (1.9 %) responded well to treatment but had recurrences, and four (2.5%) exhibited side effects definitely attributed to the medication.

Acute bronchitis was diagnosed in one third of the patients and, in these patients, therapeutic response seemed least favorable. Treatment failures were recorded in 14 (26%) of the bronchitis patients, all of whom were cured following a change to another antibiotic.

Erythromycin was surprisingly effective in patients with tonsillitis, since penicillin is generally considered to be the treatment of choice for this condition. Of the 25 patients with tonsillitis, five were classified as treatment failures. However, two of these cases were so recorded due to gastrointestinal side effects, and another was considered to be of viral etiology. The other two cases were recurrences; one was cured following an additional course of erythromycin therapy and the other occurred in a patient whose tonsils were so badly diseased as to require tonsillectomy.

Summary and Conclusions

Erythromycin stearate and ethyl succinate were used to treat 159 outpatients having a total of 170 clinical diagnoses. Clinical cures were effected in most patients. Analysis of the treatment failures indicated that the antibiotic is less effective against acute bronchitis than the other "office" infections treated.

It is concluded that erythromycin is effective against most infections encountered in routine office practice. Side effects with the preparations used were shown to be relatively infrequent.

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Consideration for others can be the thermometer to one's culture.

— Marie Wilson Garvue, R.N.

Recognition and Treatment of Acute Vascular Problems

Associated with Fractures

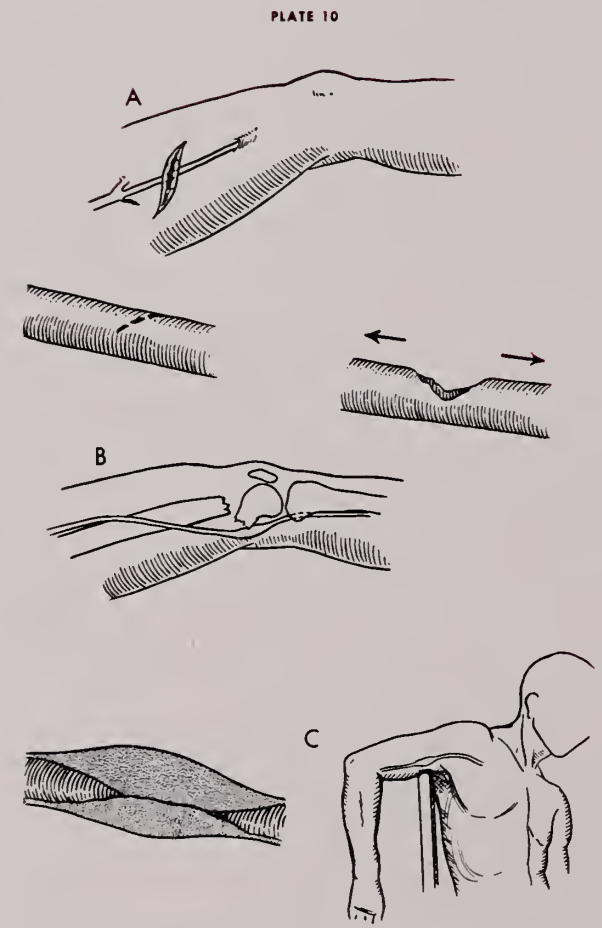

Fig. 1 — Types of Arterial Trauma: A. Laceration of artery with retraction of the wound. B. Blunt trauma as produced by supracondylar fracture resulting in contusion of the artery. C. Another mechanism of blunt trauma to an artery by a blunt object striking the undersurface of the arm. The intramural hematoma formation is illustrated.

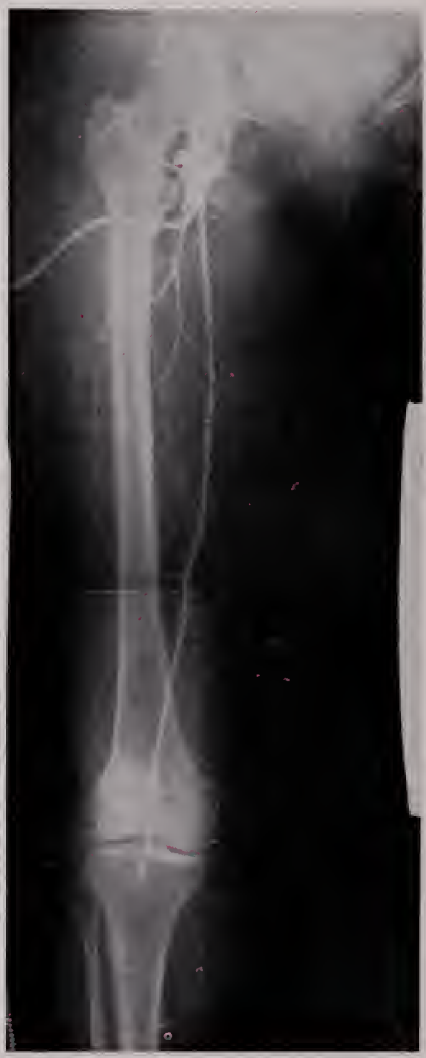

Fig. 2 — Arteriogram: Femoral arteriogram showing occlusion of popliteal artery secondary to blunt trauma.

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ACUTE VASCULAR injuries may be divided into two categories: first, those producing actual injury to the artery or veins, and second, those in which no actual direct injury to the vessel itself occurs, but the symptoms presenting are those of vascular insufficiency.

Injuries to the artery may be in the nature of contusion with thrombosis, actual laceration, or complete separation of the vessels. Various mechanisms producing these types of lesions are illustrated in Figure 1. Of these three, the most important clinically is contusion. This injury may result from blunt trauma without any obvious trauma to skin (Figure 1c); it may also occur in bumper injuries. Injury to the bone may be absent and the arterial injury overlooked. Arterial spasm is the most common diagnosis under the circumstances. Determination of circulation distal to the point of blunt trauma by palpation of pulses, oscillometric readings, and arteriography, if necessary, are very essential (Figure 2). The absence of external bleeding, swelling, and hematoma formation may make the diagnosis obscure. Exploration of the artery should be done if no improvement in circulation is noted after appropriate sympathetic nerve blocks.

PLATE 13

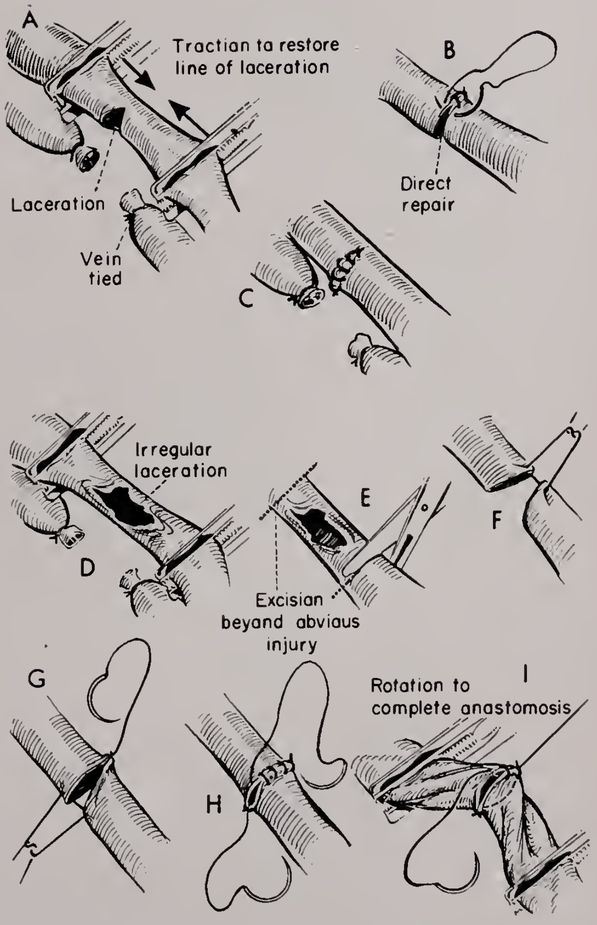
A
Traction to restore line of laceration
B
Laceration
Vein tied
Direct repair
C
Irregular laceration
E
F
D
Excision beyond obvious injury
G
Rotation to complete anastomosis
I
H

Fig. 3 — A, B and C show direct suturing of laceration of artery. D, E, F, G, H, and I.: Trauma of artery necessitating resection with either primary end-to-end suture or interposition of vein graft.

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Recognition of Arterial Injury

The important signs of the interruption of a major artery in an extremity are pallor, loss of peripheral pulses, rapidly developing anesthesia of the skin in the distal portion and loss of function of the small muscles of the hand or foot. Reflex arterial spasm also causes pallor and loss of pulses but rarely, if ever, complete anesthesia or small muscle paralysis. The effect of reflex vasoconstriction diminishes with relief of the pain by drugs and protection from motion of the fracture site. The interpretation of the finding of neurologic deficits, such as anesthesia and paralysis, will become more difficult when nerve injury is also present. Loss of sensation and motor function secondary to specific nerve interruption will have a definite and predictable pattern, whereas that associated with terminal ischemia of the part will involve it in a more general way without regard to a specific nerve distribution.

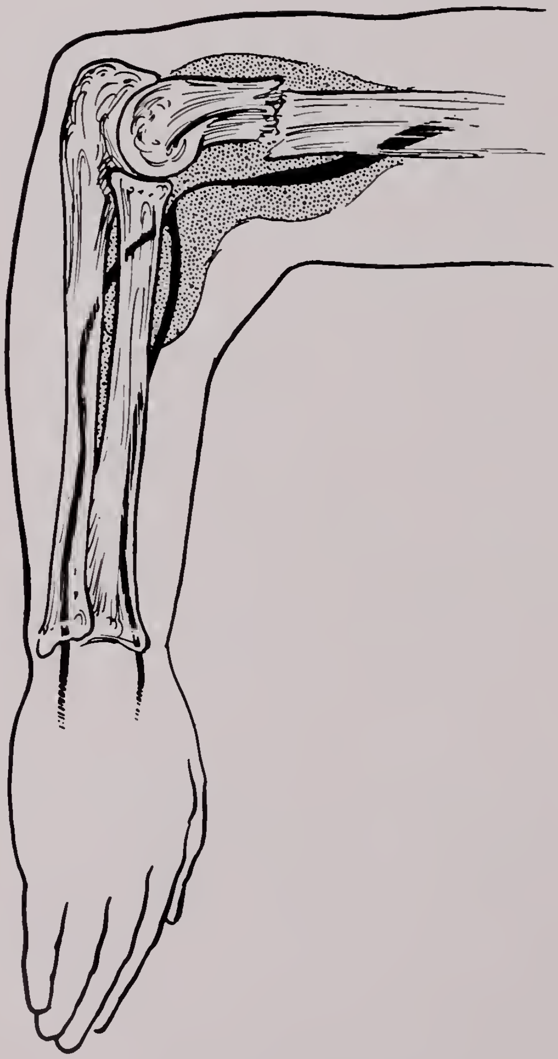

Fig. 4 — Hematoma formation following supracondylar fracture of humerus. Brachial artery is compressed as well as being in spasm.

Surgical Treatment

Surgical treatment of contusion always involves resection of the contused area, since evacuation of the clot alone will result in failure. This same principle applies to lacerated arteries where the destruction is too great for primary suture. Primary anastomosis or interposing of a saphenous vein autograft is the procedure of choice (Figure 3). When the artery is lacerated a hematoma may form, or if the artery is completely divided it may retract without too much bleeding. Where it is partially lacerated and a hematoma forms, a pulsating mass may result and present as a false aneurysm or pulsating hematoma. The history of injury and the presence of pulsating mass with a systolic bruit heard over it makes the diagnosis. In these cases resection of the involved segment is usually necessary with reconstruction of the artery by anastomosis or graft. Where both artery and vein are injured, a pulsating mass may appear with a palpable thrill. A continuous murmur is heard over the mass immediately or within hours to a few days. The presence of a continuous thrill and continuous murmur makes the diagnosis of an arteriovenous fistula. Although an arteriogram will confirm the presence of a false aneurysm or arteriovenous fistula, physical examination alone will result in a proper diagnosis in every case. The repair of this condition involves dissection of the fistula with either repair of the vein primarily or ligation of the vein, always with restoration of the continuity of the artery.

Most of the injuries to arteries associated with fractures occur when the fracture is adjacent to a point such as in a supracondylar fracture of the humerus or femur. Many of these are compound fractures, and inspection of the vessels is extremely important at the time of the primary care of the wound. Where the wound is not compound, careful palpation of distal pulses after reduction of the fracture is extremely important, as a large hematoma may result in gradual compression of the artery (Figure 4). With evidence of arterial obstruction, the brachial artery should be explored and appropriate repair done. At times, if there is extensive contusion of the entire forearm, distal thrombosis of the small vessels may prohibit successful restoration of vascular continuity. When injuries of the arteries are associated with fractures of the long bone, such as the femur, it is important that careful attention be paid to fixation of the fracture at the time of vascular repair. If traction alone is used, it is very important that the traction not be disrupted, since the vascular graft that may have been done will be endangered. Massive hematoma in the thigh from a fractured femur may indicate possible blood vessel injury. Arteriograms will help define the situation.

Complications

Ischemic Contracture

An entity that has been described for many years is that of Volkmann's ischemic con-

PLATE 4

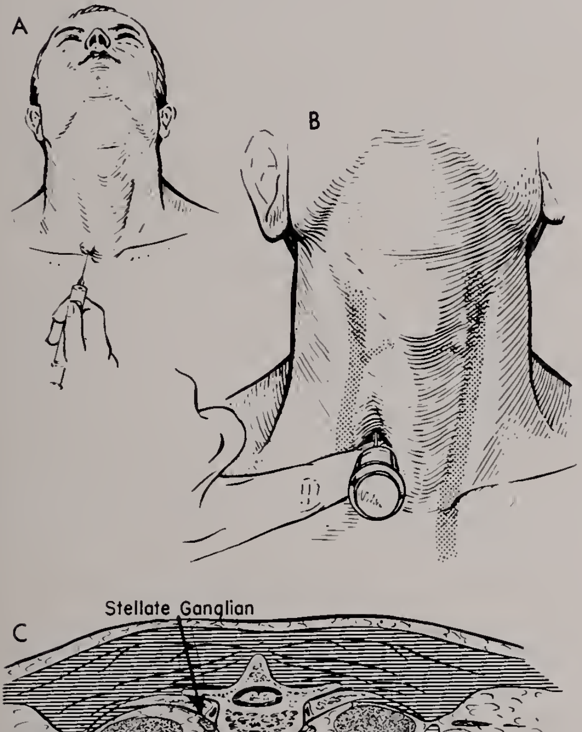

Fig. 5 — Stellate Ganglion Blocks: A and B. A 10 cc. syringe with a 2-inch gauge needle attached is filled with 2% procaine hydrochloride. The finger is used to pull the carotid vessels laterally and the needle is directed posteriorly towards the 7th cervical vertebra. C. After hitting the fascial covering of the cervical spine, the needle is withdrawn slightly and the anesthetic agent is injected.

PLATE 3

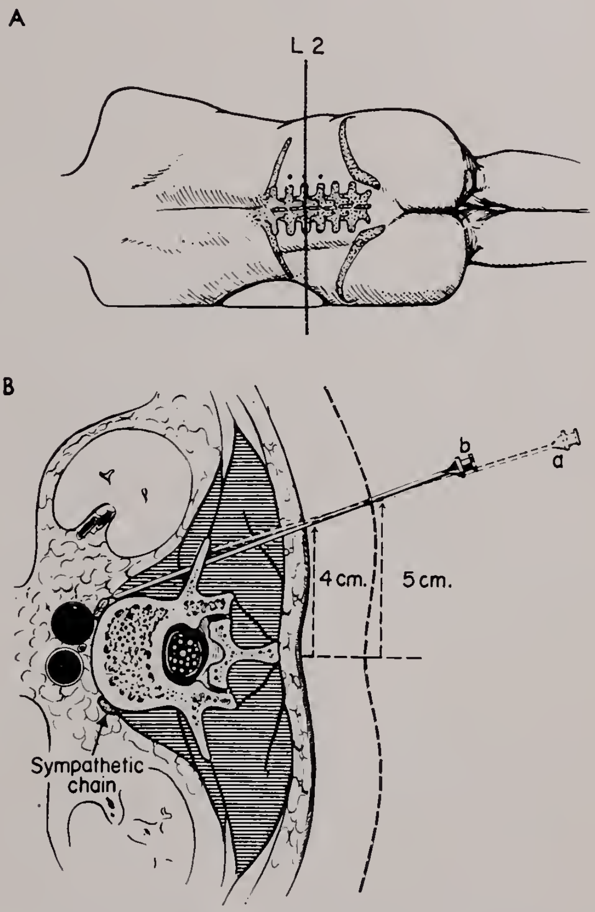

Fig. 6 — Lumbar Sympathetic Ganglion Block: A. The patient may be placed either laterally as shown, or in the prone position. Needles 7 inches long are used for the injection. B. The needle is inserted until it hits the side of the lumbar vertebra and then advanced to the anterior aspect. Injection is made in the appropriate place. The inferior vena cava on the right and the aorta on the left may be entered inadvertently. The needle is then withdrawn and injection made.

tracture. It has been chiefly noted following supracondylar fractures of the humerus or both bones of the forearm and supposedly is brought on by continued swelling after immobilization of a point in flexion. It is either related to actual damage to the artery at the time of the fracture or may be related to continued swelling inside of a case, with first venous occlusion followed by subsequent arterial occlusion with swelling and resultant obstruction of arterial supply and ischemia. The end result is the production of an atrophied forearm and useless hand. This condition in reality reflects improper management of vascular injury secondary to trauma and is preventable. Careful observation of an extremity placed in a case is important in determining any undue swelling and loss of pulses. Prompt removal of the cast may relieve the situation. Exploration with fasciotomy in an extremely swollen extremity may drain the hematoma with restoration of pulse. If the artery is in severe spasm, local application of papaverine may help; in other cases forcible distention of the artery with saline solution will result in a patent vessel. If there is any indication of contusion, then the artery must be resected and treated as outlined previously.

Post-traumatic Sympathetic Dystrophy

A final group of patients are those in whom the trauma may result in a fracture or be very minor in nature. In these patients there is no actual injury to the artery itself. The resultant series of events are those of continuing reflex vasospasm with subsequent demineralization of bone, the syndrome being known as causalgia or post-traumatic sympathetic dystrophy. As this condition is often overlooked or treated as a form of psychoneurosis, it is very important in industrial medicine. This syndrome may follow a very minor trauma to a hand, for example, or may be associated with other orthopedic conditions such as fractures of the ankle or metatarsal bones. The pain is severe and chronic in nature, aggravated at times by changes in temperature; the extremity appears cold with increased sweating. As the symptoms may be aggravated by emotional upsets, these patients are sometimes labelled malingerers. The diagnosis is made by appropriate sympathetic nerve blocks. In the upper extremity a stellate ganglion block is done with the anterior approach (Figure 5). The area is infiltrated, resulting in most cases in an adequate sympathetic nerve block. In the lower extremity a lumbar sympathetic block is done as illustrated in Figure 6. If the blocks produce relief of pain, then the diagnosis is most often that of post-traumatic sympathetic dystrophy. In some cases two or three nerve blocks may actually produce permanent relief of pain. If, however, after two to three blocks the relief of pain is still only temporary, then a sympathectomy will provide a permanent cure.

The Penalty of Overweight

Obesity can cause dyspnoea, excessive fatigue, and limited capacity for performing muscular work by increasing the body load. In all types of work, mechanical efficiency is impaired by obesity.

— Cyril M. MacBryde, M.D., Signs & Symptoms, Lippincott Co.

ANSWER TO WHAT'S YOUR DIAGNOSIS

(From page 454)

Infarct of the left fallopian tube.

The difference between a moral man and a man of honor is that the latter regrets a discreditable act even when it has worked. — H. L. Mencken

Renovascular Hypertension*

Clinical Detection

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THE DETECTION of renovascular hypertension depends first, on clues found in the clinical history and physical examination; second, on clues derived from the clinical laboratory and ordinary X-ray examinations, and finally on aortography and renal arteriography. During such an investigation, tests should be made to define if possible a specific etiology for the hypertension, whether it be renal or otherwise. Before launching such an investigation one should first be satisfied that significant hypertension is present by means of repeated blood-pressure determinations and a search for signs of high-blood-pressure effect on the heart, eyes, and kidneys.

It should be noted first of all that renovascular hypertension cannot be distinguished from essential hypertension by its severity, by its variability, by its response to rest in the hospital, or by its response to medicines, since renal hypertension may be mild or severe, may vary greatly from time to time, may decline markedly during hospital repose, and may respond well to medicines, just as does essential hypertension.[1]

History

The family history will often yield a history of hypertension among the relatives; a lower incidence may be expected in other types of hypertension. If a family history of hypertension is absent, this should make one more willing to pursue the investigation to the last degree.

Duration

The history of abrupt or recent onset of hypertension is often found in renovascular hypertension, whereas this is not so with essential hypertension.[1]

The duration of the hypertension is also of prognostic importance, since the chances of improvement with surgical relief are smaller if the hypertension has been present for more than five years.[2] However, we have seen cure result from nephrectomy performed as long as ten years after severe injury to one kidney.

Injury or Infection

A history of injury to the kidney in the past can be an important clue in some cases of renovascular hypertension. Chronic pyelonephritis is likewise a common cause of renal hypertension.[3]

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*Read before the Minnesota Radiological Society Meeting, February 29, 1964, Minneapolis, Minnesota.

If malignant hypertension is found without a prior history of a lesser degree of hypertension for a number of years, one should suspect renovascular hypertension, since malignant essential hypertension is almost always superimposed upon an essential hypertension of lesser severity of several years duration.[1]

Pain in the flank can be an important clue to the possibility of segmental renal artery occlusion, particularly in patients with a cardiac source for emboli.[1]

Age

The age of the patient is important to consider, because essential hypertension usually begins in the middle years, with the average onset in the thirties. If it begins in youth, it is not usually essential hypertension; nor is it such when the onset is in old age.[1] Both old and young patients should therefore receive careful study.

Symptom Complex

Paroxysmal headache, sweating, and pounding of the heart can be an important clue to the presence of pheochromocytoma, particularly in cases with paroxysmal elevation in the blood pressure. In patients with sustained hypertension, the absence of weight loss is strong evidence against pheochromocytoma, since weight loss associated with hypermetabolism is almost universal when pheochromocytoma produces sustained hypertension.[4] Muscle weakness and cramps, polyuria, polydipsia, paresthesias, and tetany would strongly suggest primary aldosteronism as the cause of the hypertension.[5]

Physical Examination

The Blood Pressure

The blood pressure should be measured in the leg of every patient with hypertension in the arms. It is not sufficient to palpate the femoral pulse, for coarctation with complete or nearly complete closure of the aorta with normal femoral pulses and blood pressures can be observed. If the blood pressure in the legs is not higher than that in the arms, then further search for coarctation should be made.

A severe degree of hypertensive retinopathy, with hemorrhages and exudates, may be found either in essential hypertension or renal hypertension. Its presence, however, would be strongly against the diagnosis of primary aldosteronism, since such a degree of retinopathy is rare in that disease.[5]

Carpopedal Spasm

Carpopedal spasm with a Trousseau sign upon the application of the blood pressure cuff can be an important sign indicating primary aldosteronism. This is attributable to the alkalosis which results from the excessive loss of potassium in this disease.

Bruit

A bruit over the renal arteries, usually best heard in the upper lateral abdomen, is found in some cases of renovascular hypertension, but unfortunately in a relatively small percentage.[1]

Clinical Laboratory Tests

Serum potassium and CO_2 should be determined in any hypertensive patient where primary aldosteronism is a possibility, searching for the hypokalemia and alkalosis which occurs in this disease. The finding of a persistently dilute and alkaline urine may also be a clue to the presence of aldosteronism. Even if the serum levels of potassium are not depressed to a diagnostic degree, the diagnosis may be secured by the determination of the ratio of sodium to potassium in the saliva when the patient is on a controlled diet, since aldosterone depresses the secretion of sodium in the saliva.[5]

An elevation of the blood glucose and elevation of the basal metabolic rate may be important indicators of pheochromocytoma.[6]

A much neglected simple laboratory test in hypertension is the search for cellular casts in the urine. Finding that the kidney sheds such casts is of prime importance, since this occurs only in nephritis, white cell casts predominating in pyelonephritis, and red cell casts in glomerulonephritis. Indeed, such casts may be regarded as pathognomonic of these diseases.[3]

Tests for Pheochromocytoma

In any patient where pheochromocytoma remains a possibility, either a regitine or a histamine test should be done, depending on the level of blood pressure at the time of the testing. If the blood pressure is 170/110 or above, the regitine test is sensitive and reliable if done properly. Proper conduct of the test means that antihypertensive drugs should be withdrawn for a period of two weeks, since false negative tests will otherwise be frequent. Sedatives should also be withdrawn for a period of 48 hours, since false positives will otherwise be frequent.[6] If the blood pressure at the time of the testing is below 170/110, then a provocative test with histamine should be performed, injecting 0.05 mg. intravenously, observing the blood pressure every twenty to thirty seconds thereafter. A syringe full of regitine should be attached to the needle after the histamine is injected in case it is needed to control a hypertensive reaction.

Where such testing is not definitive, the urine catecholamines, or the derivative, vanylmandelic acid, may be determined. Single normal values do not, however, rule out pheochromocytoma.[6]

Intravenous Pyelogram and Radioactive Renogram

If pheochromocytoma, primary aldosteronism, coarctation, and glomerulonephritis have not been discovered as possible causes of the hypertension, then all patients should have an intravenous pyelogram, or a radioactive renogram if this is available. The pyelogram may reveal pathology such as polycystic disease, pyelonephritis, or congenital hypoplasia to explain the hypertension. The sensitivity of the pyelogram in renovascular disease may be increased by obtaining early films without compression. It is important to look for a disparity in the time of appearance of the dye in the two kidneys, and also for any disparity in the length of the two kidneys. Either may be a sign of renovascular disease. However, normal findings do not rule out renovascular hypertension.[1,2,7,8] The sensitivity of the procedure may be increased further by comparing the speed of washout of the dye from the two kidneys after a diuresis from water or urea.[9,10]

If such a disparity is found on the intravenous pyelogram or the radioactive renogram, then aortography is obviously indicated. Even if the pyelogram and renogram are negative, aortography should nevertheless be performed in the following patients: the young patient, the old patient, the patient with recent onset of hypertension or abrupt onset or acceleration of hypertension, the patient with a bruit over the renal artery or with a history of injury to the kidneys, the patient without a family history of hypertension, and in all patients who have malignant hypertension.

Using all of these criteria for selection of patients for aortography, very few patients with renovascular hypertension will be missed.[1] If renovascular stenosis is found, but the significance of the arterial lesion is in doubt, measurements of pressures distal to the lesion,[10] or differential function studies of the two kidneys, may help settle the question of whether the lesion is producing the hypertension.[11] Since differential function studies are indirect indicators of whether the kidney is producing pressor agents, no perfect correlation is to be expected. A reliable method for measurement of renal pressor agents from the individual human kidney would be the definitive measure of the pathologic physiology.[12]

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Blood Alcohol from Corpse Admissible*

Intoxication tests on blood obtained from a corpse were held admissible in a passenger's suit against a bus company. The injuries to the passenger were sustained when the bus collided with an automobile. Evidence that the driver of the automobile was intoxicated was admissible even though the intoxication test was made of blood obtained from the body of the deceased driver. Evidence of the blood test was given by a pathologist, whose duty it was to investigate deaths for the county coroner. He testified that he drew blood out of the driver's heart after he had expired. A test of the blood showed .35 grams of alcohol per 100 millimeters of blood, indicating intoxication.

The supreme court of Missouri refused to rule on the passenger's contention that obtaining the blood from a corpse amounted to an unconstitutional search and seizure. The bus passenger contended that evidence of the blood test should not have been admitted because it was obtained by unlawful and criminal desecration of a dead body, repugnant to common ideas of decency, amounting to unconstitutional search and seizure. The court said that the bus passenger had no standing to raise the question since the constitutional right to freedom from unlawful search and seizure is a personal one, and there was no relationship between the automobile driver and the bus passenger.

Diener v. Mid-American Coaches, Inc. 378 S. W. 2d 509 (Mo., Apr. 13, 1964)

Editor's Note: Alcohol levels for determining intoxication can be made on the breath, the urine, and the blood, and can be interpreted in relation to the blood alcohol value. The urine value is 1.3 times that of the venous blood, and the breath (alveolar air) has a ratio of 2100 to 1. From these figures, the equivalent amount of alcohol in the blood can be calculated. In order that a 150 lb. man reach a blood alcohol level of .15, it would be necessary for him to drink approximately 6 ounces of 100 proof liquor. One bottle of beer (8 oz.-6%), one glass of wine (4 oz-20%), and one ounce of whiskey (100 proof-50%) provide approximately equal quantities of alcohol.*

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*Committee on Medical-Legal Problems, JAMA 170:47, 1959

April Saints and Medicine

Familiar as an April saint is Bernadette (1844-1879), identified with the shrine at Lourdes, France, the healing powers of whose grotto waters were revealed to her as a young girl by the Virgin Mary. This shrine became world-famous and continues to this day to be a Mecca for the ailing who believe in the curative properties of its waters and are sometimes mysteriously and inexplicably benefited thereby.

St. Bernadette's commemorative day is April 16.

Drinking a little too much is drinking a great deal too much. — German proverb

The word impossible is not in my dictionary. — Napoleon

The Surgeon's Role in Renovascular Hypertension*

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RENOVASCULAR HYPERTENSION has its basis in a mechanical derangement and thus falls into the category of problems with which the surgeon deals most effectively. Our present understanding of this problem is based on the astute observations of Bright[1] at the autopsy table, the brilliant laboratory study of Goldblatt,[3] and the clinical application of knowledge accumulated to 1954 by Freeman,[2] who diagnosed renal artery obstruction by aortography and cured his patient's hypertension with thromboendarterectomy. An indication of the rapid development in this field is the fact that Poutasse[6] wrote in 1956 that the proper treatment for a patient with hypertension due to renal ischemia is nephrectomy. Yet this same author was responsible for stimulating interest in corrective surgery for renovascular hypertension by his report in 1959 of a series of cases successfully treated by arterial reconstruction.[7]

The surgeon leans heavily upon the angiogram in planning and executing renovascular reconstructive procedures, much as he depends on accurate mapping of each of the segmental bronchi of both lungs in planning the surgical treatment for bronchiectasis. He is now often content to have an adequate film of the main renal arteries but will in the future be asking for ever more perfection in demonstrating the entire renal arterial tree on both sides. It is possible to restore arterial flow through reconstructive procedures to vessels the size of the anterior or posterior tibial artery in the leg. Thus it does not seem unreasonable for us to expect to be able to reconstruct individual renal segmental arteries.

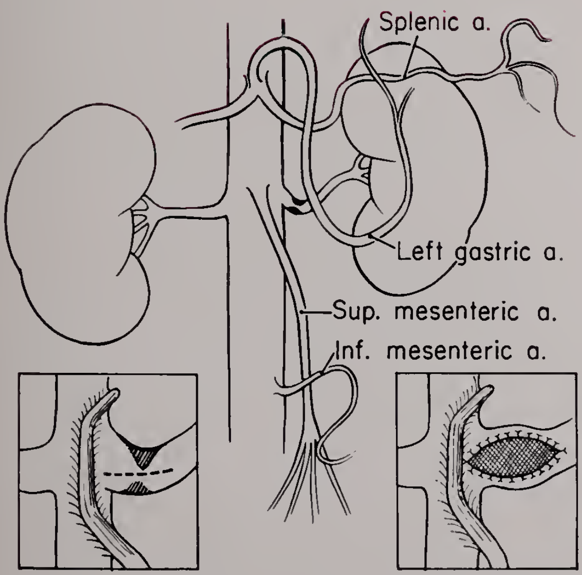

Fig. 1 — Diagram of method of renal artery reconstruction employed in our first patient, who was operated upon in July, 1960, at age 39. His malignant hypertension was corrected and he remains normotensive to this time.

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*Read before the Minnesota Radiological Society Meeting, February 29, 1964, Minneapolis, Minnesota.

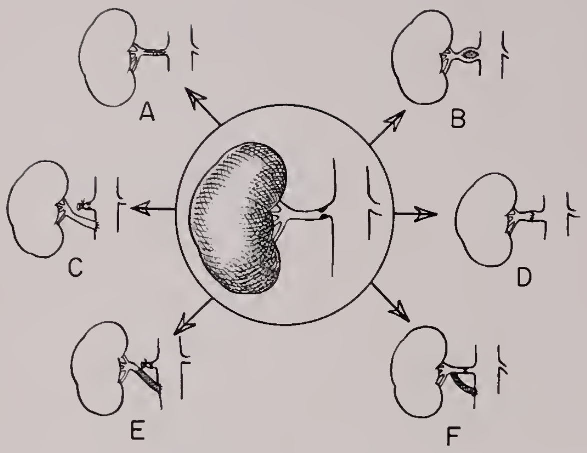

Fig. 2 — Diagram of some of the methods available for reconstruction of the renal artery. a. Endarterectomy. b. Patch graft. Vascular prosthetic material or autogenous vein may be used as the patch. The latter is preferred. c. Reimplantation of renal artery to side of aorta. d. Excision of obstructed segment and end-to-end anastomosis. e. Vascular prosthetic or autogenous vein graft from aorta with end-to-end anastomosis. f. Graft (prosthetic or autogenous vein) from aorta to side of renal artery.

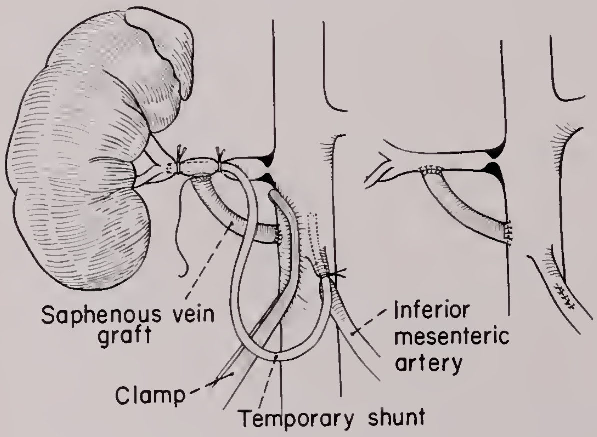

Fig. 3 — Diagram of method using a temporary external shunt to maintain blood supply to the kidney during the period necessary to construct the permanent bypass. This eliminates the need for hurry and permits the fine techniques applicable to autogenous vein grafts and mandatory in reconstruction of small arteries.

Available Surgical Techniques

Corrective surgery implies that the basic mechanical problem be remedied with preservation of all possible functioning parenchyma. Nephrectomy cannot be considered a corrective procedure for this disorder, even though it could relieve the hypertension. Some of the techniques available to the surgeon are illustrated in Figures 1, 2 and 3. The aim at operation is to restore a pulsatile flow at aortic pressure to the renal arterial system.

The incision is mid-line from the xiphoid to the pubis. Complete exploration of the abdominal cavity is carried out with palpation of the adrenal glands, at the least. A needle biopsy is taken from each kidney so that the extent of parenchymal disturbance can be used as a guide in the future management of the patient. The pressure is measured in the aorta and in the renal artery distal to the obstruction. It is arbitrarily stated that those patients who have 40 mm. of mercury less pressure in the renal artery than in the aorta will have good results from arterial reconstruction. Those who have no gradient have nothing to gain from arterial reconstruction and should therefore not be subjected to the risks of this procedure.

Having assessed the local pathology, and having correlated this with the preoperative angiogram, the plan of arterial reconstruction is made. The choice of procedure will depend on the individual mechanical problem to be dealt with and the surgeon's preference based on his experience with the methods available.

Instituting Diuresis

At this point an intravenous drip of 25 to 50 grams of Mannitol in a 10 or 20 per cent solution is started, because there is evidence that this osmotic diuretic is of value in assisting the kidney to recover from ischemia.[5] The patient is given 1.5 to 2.0 mg. per kilo of heparin intravenously to avoid clotting during the time of reconstruction.

Interrupting Blood Supply to Kidney

The actual reconstructive procedure is planned so that the kidney will be without blood supply for as short a time as possible. It apparently is the practice of the majority of surgeons to interrupt renal arterial flow completely during the period of reconstruction. All will make this period as short as possible, but Poutasse and others will accept thirty minutes of total ischemia without concern. There is no doubt, however, that the time factor does put emphasis on speed. Total body hypothermia may be employed to extend the tolerable ischemia time, but this method has some inherent problems which limit its usefulness. It would, of course, be ideal if the ischemia time were zero. To this end we have used temporary external and internal shunts (Fig. 3), which have proved eminently satisfactory in our reconstruction of the extracranial cerebral arteries where, if the tolerable ischemia time is exceeded, the effect is so distressing and immediately apparent.

Hyperbaric Oxygenation

Hyperbaric oxygenation will extend the tolerable ischemia time also, and it undoubtedly will find application in renovascular surgery for the solitary kidney and those cases with bilateral renal artery stenosis with renal failure.

Partial Nephrectomy

Partial nephrectomy may be effective in reducing the hypertension when a segmental artery unsuitable for reconstruction is involved. In those cases where arterial reconstruction is not possible, or has failed for some reason, nephrectomy may still be employed in treatment of the hypertension. It should not, however, be chosen as the initial procedure any more than amputation of an extremity for a gangrenous digit should now be undertaken without obtaining angiograms and considering the possibility of arterial reconstruction.

End Results

The number of cases in our personal series and the duration of follow-up does not permit valid statistical analysis. Morris et al.,[4] 1963, had a series of two hundred cases with follow-up from three months to five years. Their patients ranged in age from eight to seventy-two years. Sixty-five per cent were males. Hypertension was present for less than five years in sixty-five per cent. Arteriosclerosis accounted for the obstruction in eight-five per cent and fibromuscular hyperplasia in thirteen per cent. The stenosis involved the proximal third of the renal artery in seventy-five per cent. Renovascular reconstruction resulted in the blood pressure returning to normal in eighty per cent and decreasing significantly in another eight per cent. Such results speak well for Morris' careful selection of patients as well as a skillfully executed reconstruction.

Of great interest is the fact that twelve of these patients were operated upon for renal failure. Carefully done aortograms had revealed bilateral renal artery stenosis. In this seriously-ill, high-risk group, arterial reconstruction was undertaken with only one surgical death. The remaining eleven patients were reported to have improved renal function, and the hypertension was said to be controlled in the majority.

Summary

Dependence upon the accuracy of the preoperative angiogram and our growing experience with improved surgical technique will demand increasing perfection in angiographic mapping.

It would seem from the report of Morris that we must now consider for renal angiography and possible arterial reconstruction certain selected patients with chronic renal failure.

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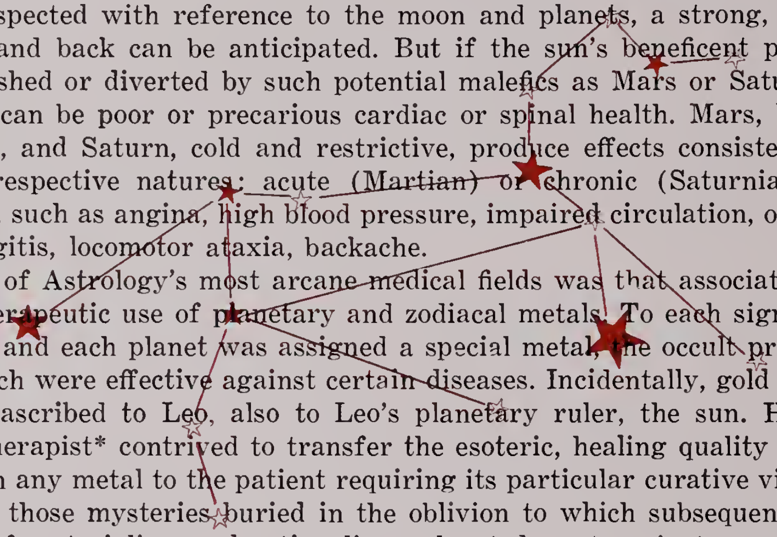
Astrology and Medicine — Leo, the Lion

The constellation of Leo, the Lion, is familiar to many an amateur stargazer in the northern hemisphere for its royal prominence in the zodiac during the spring months. Since the sun occupies this sign from about July 22 to August 22, any individual born between these dates is a Leo native.

Astrologically Leo governs the heart and circulatory system, also the spinal cord and column. If, at the time of a native's birth, the sun is favorably aspected with reference to the moon and planets, a strong, healthy heart and back can be anticipated. But if the sun's beneficent power is diminished or diverted by such potential malefics as Mars or Saturn, the result can be poor or precarious cardiac or spinal health. Mars, hot and violent, and Saturn, cold and restrictive, produce effects consistent with their respective natures: acute (Martian) or chronic (Saturnian) disorders, such as angina, high blood pressure, impaired circulation, or spinal meningitis, locomotor ataxia, backache.

One of Astrology's most arcane medical fields was that associated with the therapeutic use of planetary and zodiacal metals. To each sign of the zodiac and each planet was assigned a special metal, the occult properties of which were effective against certain diseases. Incidentally, gold was the metal ascribed to Leo, also to Leo's planetary ruler, the sun. How the astrotherapist* contrived to transfer the esoteric, healing quality crystallized in any metal to the patient requiring its particular curative virtues is one of those mysteries buried in the oblivion to which subsequent incursions of materialism and rationalism relegated most ancient, secret practices.



High in the southern sky at mid evening in April Leo is fully visible in its regal splendor, proceeding westward. The six bright stars delineating the forepart of the Lion are known as the Sickel, the brilliant 1.3 magnitude star, Regulus, marking the end of the handle.

From the astrological identification of Leo with the heart derive the adjective 'lion-hearted'; the appellation 'Coeur de Lion'; and the name 'Leonard.'

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*See Test Your Word Score, Page 485.

I expect to spend the rest of my life in the future, so I want to be reasonably sure of what kind of future it's going to be. That is my reason for planning.
— Charles F. Kettering

If the government becomes a lawbreaker, it breeds contempt for the law; it invites every man to become a law unto himself. — Justice Louis Brandeis

Even the ugliest human exteriors may contain the most beautiful viscera.
— J. B. S. Haldane

The Value of Arteriography in the Assessment of Renovascular Hypertension[*]

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STEPHEN A. KIEFFER, M.D.[†]
Minneapolis, Minnesota

RENAL ARTERIOGRAPHY is one of the most important diagnostic procedures in the work-up of patients with suspected renovascular hypertension. With the newer transfemoral catheterization techniques, the procedure carries a negligible risk. The main value of renal arteriography lies in the exclusion or anatomic demonstration of lesions which may cause renovascular hypertension. However, it must be emphasized that the demonstration of such a lesion does not establish it as the cause of the patient's hypertension; in all cases, the angiographic findings must be correlated with other clinical data.

Indications

It is our feeling that renal arteriography is indicated in all patients with suspected renovascular hypertension on the basis of clinical history, intravenous urogram, and isotope renogram. Delineation of the renovascular tree not only establishes the presence of a localized correctible lesion; it also aids the surgeon in planning a corrective procedure and allows evaluation of the contralateral renovascular tree, which is occasionally involved by the same process but whose abnormal physiology may be masked by the more predominant lesion.

Postoperative evaluation following corrective surgery is another frequent indication for arteriography, especially if surgical correction should fail to reduce the patient's blood pressure.

Techniques

Aortography can be performed by the intravenous, translumbar, and transfemoral routes. The latter is by far the procedure of choice. Its advantages include the low morbidity of the Seldinger percutaneous catheterization technique,[1] local anesthesia, and the use of large lumen catheters to deliver an adequate bolus of contrast medium very rapidly, thus allowing excellent visualization of all renal arteries even in patients with very rapid blood flow. In addition, with this technique the patient can be easily positioned for oblique projections, which are so valuable in the diagnosis of fibromuscular hyperplasia and atherosclerotic stenosis of the ostium of the renal artery. Its flexibility is further emphasized by its ability to replace the straight aortic catheter with a curved-tip catheter for selective renal artery studies.

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[*] Read before the Minnesota Radiological Society Meeting, February 29, 1964, Minneapolis, Minnesota.

From the Department of Radiology, University of Minnesota Hospitals, Minneapolis, Minnesota.

[**] Associate Professor of Radiology.

[†] Medical Fellow in Radiology. National Heart Institute Trainee in Cardiovascular Radiology.

In older patients with severe atherosclerosis and tortuous iliac arteries where the retrograde passage of a catheter may be impossible, translumbar catheterization[2] is preferred. The aorta is punctured percutaneously in classical fashion under local anesthesia with a needle-catheter combination. Once the aorta is entered, the needle is removed, leaving the Teflon catheter in place. This catheter is then advanced in the aorta, allowing the use of a power injector without danger of subintimal injection. Injection is made during the Valsalva maneuver, thus decreasing cardiac output and enhancing contrast visualization of the distal aorta and its branches. Nevertheless, the diagnostic quality of aortograms obtained by translumbar catheterization is inferior to studies made by the transfemoral approach. Furthermore, hematoma formation near the prospective operative site cannot be avoided.

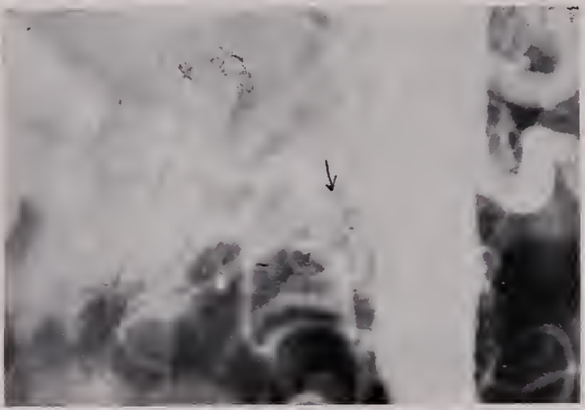

Fig. 1 — Renal artery stenosis due to atherosclerotic plaque. A. Demonstration of lesion on aortogram. B. Hemodynamic significance proven by pressure tracing during catheter pullback across area of stenosis.

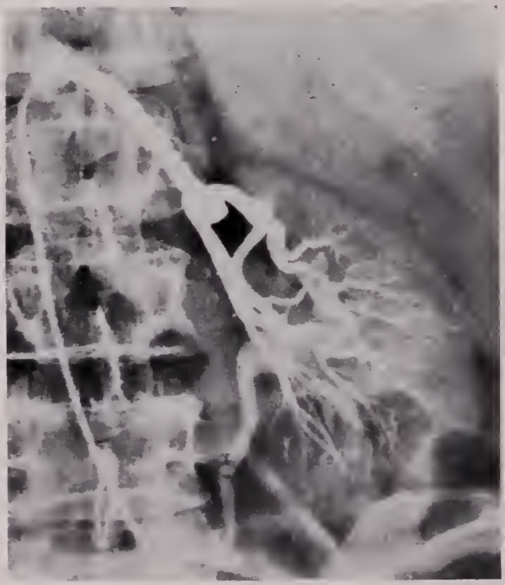

Fig. 2 — Fibromuscular hyperplasia. Typical accordion-like beading of renal artery.

Intravenous aortography does not yield sufficient concentration of contrast medium in the renal arteries for satisfactory interpretation of renovascular hypertension. Therefore, there is no place for this technique in the evaluation of renovascular hypertension.

Selective Renal Arteriography

The initial procedure should always be an aortogram, since this procedure allows visualization of the entire renal vascular tree on both sides. In addition, segmental renal arteries have been found to be of such frequent occurrence that an aortogram is mandatory in all cases.

However, once a vascular lesion has been seen, especially if it is of questionable nature, it is helpful to selectively catheterize the involved renal artery and obtain another arteriogram to eliminate disturbing superimposition of other arterial branches.

In addition, it may be possible to pass a minute catheter across the area of stenosis in order to record pullback pressures. This latter procedure is of particular value in the exclusion of hemodynamically insignificant lesions, thus eliminating unnecessary surgery.[3] Such a procedure requires considerable skill and carries the risk of postcatheterization thrombosis of the renal artery or its branches. Its use should be limited to patients with mild renal artery stenosis and otherwise normal clinical tests.

Angiographic Findings

The vast majority of patients with curable renovascular hypertension show obvious angiographic findings, usually consisting of marked narrowing of the main renal artery or its segmental peripheral branches.

Atherosclerotic Plaque

The most common cause of stenosis is atherosclerotic plaques. These occur in the older age group and are frequently found at the ostium of the renal artery or in its proximal third (Figure 1). The lesion appears as an eccentric "filling defect," which is especially well appreciated when seen in profile. Plaques seen "en face" appear only as areas of slightly decreased density, and can therefore be easily overlooked unless examination is repeated in an oblique projection. Occasionally, atherosclerosis will cause a diffuse narrowing of the artery. Stenotic atherosclerotic lesions may be seen in patients who are normotensive and in those who have essential hypertension; no patient should therefore be operated upon on the basis of the aortogram alone.

Fibromuscular Hyperplasia

Perhaps the second most common cause of renal artery narrowing is fibromuscular hyperplasia (Figure 2), a lesion that occurs in a younger age group. The typical angiographic finding is multiple areas of concentric narrowing. Between these narrow ridges or septa, there are areas of relative dilatation producing a beaded appearance. In about half of the cases, the lesion is bilateral. It is usually found in the middle and lateral thirds of the renal artery and may extend into smaller branches.

Coarctation of Renal Artery

Less commonly, congenital stenosis or coarctation of the renal artery may be

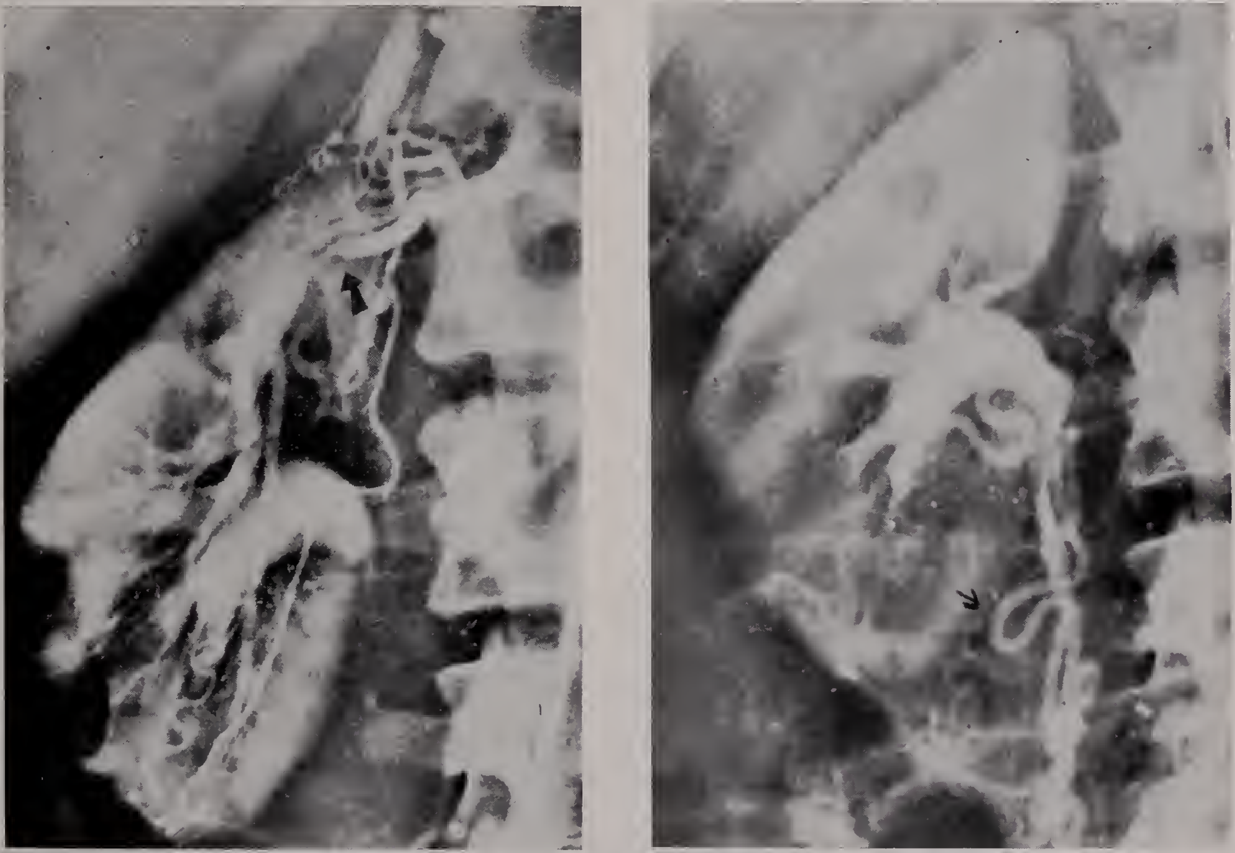

Fig. 3 — Complete occlusion of renal artery, likely congenital. (a-left) Demonstration of occlusion. (b-right) Collateral supply through ureteric artery. Contrary to common belief, complete occlusion of the renal artery with collateral supply may cause renovascular hypertension. This patient also had a positive urea washout urogram and was cured of her hypertension by surgery.

demonstrated. This is usually seen in children and young adults and has been considered by some investigators as a manifestation of fibromuscular hyperplasia. However, the angiographic appearance is quite different, since only a single area of concentric narrowing can be found (Figure 3).

Perinephric Disease

Perinephric constrictive disease, such as perinephric hematoma and fibrosis, may be a rare cause of curable renovascular hypertension. Thus, angiographic failure to demonstrate renal artery stenosis does not exclude the possibility of curable renovascular hypertension.

Pyelonephritis

In rare instances, pyelonephritis with scarring of renal parenchyma may result in ischemic water reabsorption and true curable renovascular hypertension.[4] It should be noted that the vast majority of patients with pyelonephritis and hypertension do not have curable disease.

Renal Artery Infarct

Renal artery infarction, although rarely followed by hypertension, may be well demonstrated angiographically. The occluded vessel may be evident on a study of high quality; selective renal arteriography is preferred because of its greater diagnostic accuracy.

Summary

Because it allows definite exclusion or anatomic delineation of lesions causing curable renovascular hypertension, renal arteriography is a most important diagnostic procedure. Transfemoral catheterization of the aorta is the technique of choice. Angiographic demonstration of renal artery narrowing alone does not imply curable hypertension; in all cases, the angiographic findings must be correlated with other clinical data.

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*Leff, S., M.D., D.P.H.: From Witchcraft to World Health. The MacMillan Co., New York, 1958, p. 70.

In our precious cabbage patches the holometabolous insecta are the hosts of parasitic polyembryonic hymenoptera, upon the prevalence of which rests the psychic and somatic stamina of our fellow countrymen. — William Osler

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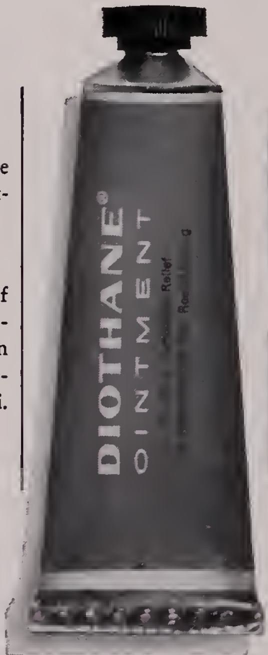

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Editorials

Avulsion of Large Portion of the Scalp*

THE IMMEDIATE care of patients who have lost a large portion of the scalp involves the usual measures of controlling shock, hemorrhage, and pain. However, of special importance in this type of traumatic injury is treatment directed toward early skin coverage of the denuded cranium, thus preventing unnecessary scarring; this is especially true of the forehead where the eyelids can be severely distorted by cicatricial contractures. Ectropion of one or both upper eyelids is rather common when the application of skin grafts to the forehead is delayed; in fact, cases have been reported in which the ectropion was so severe that exposure of the globe resulted in loss of the eye. Occasionally, circumstances may be such that it is inadvisable to skin-graft the entire cranium in one operation; if such is the case, it is always preferable to skin-graft the forehead first, thus preventing in great measure the development of scar tissue that would distort the upper eyelids.

In cases of avulsion of a large part of the scalp, if raw surfaces and exposed bone are not covered with skin grafts but are allowed to granulate slowly and epithelialize spontaneously, the resultant scar tissue has a tendency to break down easily under the slightest trauma and to form an ulcer that may require weeks or months to heal. In addition, the possibility is always present that these scarred zones may undergo malignant degeneration.

In debriding the type of scalp wounds being discussed, shredded pieces of tissue are removed, loose flaps of skin around the periphery of the injured region are replaced and sutured, and torn bits of pericranium are unrolled, replaced, and sutured with fine catgut. Without waiting for a granulating surface to develop, I have found it helpful to proceed immediately with the application of split-thickness skin grafts obtained from the abdomen or thighs, providing that most of the periosteum is still intact. Moreover, if the wound can be grafted within a few hours after the injury, I do not hesitate to place thin split-thickness skin grafts directly over exposed bone even though some of the pericranium may have been lost. Fortunately, the greater part of such grafts usually takes satisfactorily.

If a patient with avulsion of large parts of the scalp is not seen for several days after the injury, free skin grafts applied directly over exposed bone and nonviable periosteum is inadvisable. In such cases, many surgeons believe that it is best either to drill holes into

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*McFee, A. S., Fisher, J. C., and Peyton, W. T.: Loss or Destruction of the Scalp—Report of Two Cases, Minnesota Med 47:1468, 1964.

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the outer table of the denuded cranium or to chisel down the cortex until a bleeding surface is obtained. By such technics, bleeding areas lead to the development of granulations that grow to eventually cover all of the exposed bone. However, waiting for the development of such a granulating surface before skin grafts can be applied requires weeks or months, during which time dense scar tissue sometimes forms. Furthermore, when the entire wound is allowed to granulate before skin grafts are applied, the grafted areas often do not possess a smooth appearance but are rough and irregular. Instead of waiting for a granulating surface to appear, it often is preferable to chisel down the outer table of the cranial cortex until active bleeding is encountered, after which split-thickness skin grafts can be immediately applied. These grafts usually take well and result in a smooth, cosmetically acceptable surface. It is true, of course, that skin grafts placed directly on bone do not prevent sequestration of small zones of osseous tissue, which may come away as small spicules of dead bone weeks or months later.

Some surgeons advocate pedicle flaps of skin to cover the denuded cranium. However, skin flaps probably are best employed only after split-thickness skin grafts have been applied. Such grafts get rid of raw surfaces and consequently infection in the wounds. Moreover, in most cases, the split-thickness grafts make a satisfactory coverage, thereby eliminating the lengthy process of preparing pedicle flaps of skin.

John B. Erich, M.D.
Rochester, Minnesota

Pneumomediastinum

IN REFERENCE to the article on Subcutaneous Emphysema by R. B. Tudor and Pablo Ramos* appearing in the November issue of MINNESOTA MEDICINE, certain comments seem apropos.

In adults, subcutaneous emphysema of the neck occurring secondary to mediastinal emphysema is most commonly due to perforation of either the major airways or the esophagus. This results from trauma to the thorax, during endoscopic or other surgical procedures, or as a result of foreign bodies.

Although spontaneous interstitial emphysema of the lung resulting in mediastinal and subcutaneous emphysema has been seen during labor, it is rarely recognized in the adult and appears to occur oftener among children with asthma and occasionally in the newborn. Undoubtedly this condition occurs many times without being recognized.

A clue to the presence of a pneumomediastinum on physical examination is a crunching sound heard synchronously with the heartbeat (Hamman's sign) on auscultation over the sternum. When the air spreads to the subcutaneous tissues of the neck it can be detected by gentle palpation.

Mediastinal emphysema can be recognized radiographically on the posteroanterior view of the thorax as a layer of air between the pericardium and the parietal pleura. On the lateral view increased radiolucency of the anterior mediastinum is apparent with retrodisplacement of the heart at times. The thymus may be more clearly outlined and there may be evidence of air extending up into the neck.

Obviously there must be a gradient in pressure which causes air, once it has escaped from the alveolus, to find its way along peribronchial and perivascular tissues to the mediastinum and often ultimately to the subcutaneous tissues. If we assume that mediastinal and intrapleural pressures are equal, this alveolar-mediastinal gradient approximates 5 to 10 cm. of water pressure during quiet breathing. Since, during quiet breathing, the mediastinal pressure is negative, air will not ascend initially to the subcutaneous tissues of the neck where pressure will be

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*Tudor, R. B., and Ramos, Pablo: Subcutaneous Emphysema. Minnesota Med 47:1339, 1964.

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considered as being at atmospheric level. Indeed, the flow of air will be from the neck to the mediastinum, as is sometimes seen during tracheostomy or laryngeal operation, particularly if there is inspiratory obstruction. However, when the intrapleural-mediastinal pressure is increased above atmospheric pressure, as in asthma, coughing, or straining, the gradient between alveolar and mediastinal pressures will be no greater but there will be a definite gradient favoring the escape of air to the subcutaneous tissues of the neck. If such escape is not adequate, the mediastinal pressure will increase and impair venous return and, thereby, cardiac output. This situation demands prompt treatment consisting of needle aspiration of the mediastinum or surgical incisions above the clavicles to release the air as described by the authors. It is also apparent why treatment to decrease airway resistance, coughing and straining is helpful.

Norman G. G. Hepper, M.D.
Rochester, Minnesota

Solid Carcinoma with Amyloid Stroma

A case report in the January issue* calls attention to a rather uncommon type of thyroid carcinoma variously called solid carcinoma or medullary carcinoma with amyloid stroma. First described by Hazard in 1959, it is now a clearly defined subtype of thyroid carcinoma of a moderate degree of malignancy. During the past decades, classification of thyroid carcinoma has varied from undue complexity to oversimplification. In 1921, Wilson described no fewer than 17 cell types of thyroid cancer. More recently, many clinicians have grouped all thyroid carcinomas into two types: a slowly growing, rather innocuous variant and a rapidly growing, almost uniformly fatal form of the disease. Pathologists now recognize four main patterns of behavior in thyroid cancer.

The commonest type, papillary cancer, is seen especially in children and young adults. This tumor is frequently very invasive, spreading throughout much of the gland, and is often associated with massive bilateral lymph node metastasis. The tumor may actually spread directly through the thyroid capsule into adjacent structures such as the larynx or the trachea. Distant metastasis occurs rarely—usually in the form of a diffuse pulmonary infiltrate. In spite of this marked tendency toward extensive thyroidal infiltration and massive nodal metastasis, the disease is remarkably curable by surgical therapy. Very few deaths from this type of carcinoma have been documented, particularly in the younger age group.

A second form of carcinoma, usually slowly growing, is the encapsulated angio-invasive tumor often called follicular carcinoma. This variant only rarely involves regional nodes but spreads via the bloodstream to bones or lung. The prognosis is excellent in cases in which vascular invasion is minimal. For patients with marked invasion, the outlook is much more serious although the rate of growth of the tumor is frequently slow.

Anaplastic carcinoma, a term used to include a number of microscopic patterns, represents one of the most serious forms of cancer in humans. Almost all cases terminate fatally, usually in a matter of months.

Solid carcinoma with amyloid stroma is classified midway between the curable papillary carcinoma and the rapidly fatal anaplastic type. As in papillary carcinoma, the growth rate may be extremely slow, and regional lymph nodes usually are involved, sometimes extensively. In the gland itself,

Continued

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*Minnesota Med 48:40, 1965.

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the tumor is circumscribed but not encapsulated and, as in papillary cancer, a clinically occult primary focus with positive palpable nodes may be present. Distant blood-borne metastases especially to viscera such as the liver are fairly common. Thus, the tumor is a much more dangerous disease than is papillary cancer. In the author's experience, approximately one third of all patients seen have died of their disease.

The surgical pathologist should be aware of the rather unique microscopic pattern of this carcinoma, either in a primary thyroid tumor or in a metastatically involved cervical node removed for diagnosis. The solid architecture with its absence of papillary structure or follicle formation may lead to an erroneous diagnosis of anaplastic carcinoma, resulting perhaps in failure to perform a potentially curative surgical procedure; or in the case of an involved cervical lymph node and a small or impalpable primary tumor in the thyroid, a needless search may be made looking for another more distant primary site.

Lewis B. Woolner, M.D.
Rochester, Minnesota

Reference

1. Ritchie, W. P., Jr., and Castaneda, A. R.: Solid Cell Carcinoma of the Thyroid With Amyloid Stroma. Minnesota Med 48:40, 1965.

Trauma and Social Conscience

THE ANATOMY of trauma is infinitely complex and touches us all. Male or female, hale or frail, no one of us lives free of the risk of accidental injury. Among increasing numbers of other bodies, we move about our world never knowing when the carelessness of one of us may lead to the damage of another of us. In this sense, each of us must be our brother's keeper. Prudent behavior must become an increasing part of social conscience.

This need is demonstrated on a nearby page, in the illuminating study by Doctors Gustilo, Foss, Leslie and Telander.[1] Accidents involving light-weight, highly-powered motorcycles have had an astounding increase in our metropolitan community. These motorcycles are usually rented, commonly by youngsters, who may be more or less rash and who lack the skill and experience needed for safe operation. Many of those injured are riding for the first time. Many of the injuries are severe, and frequently they are multiple.

As you read this article, consider the sum of years of lost life and of residual disabilities in the survivors of this group of young people. Question how many other citizens may have been injured in the forty-six accidents involving automobiles. Estimate the dollars of expense, the days and weeks of pain and anguish, the months and years of legal proceedings. Ask yourself how many of these accidents might have been avoided by even the simplest of safety precautions: Adequate instruction in the peculiar dangers of these machines.

The winter season enforces prudence in motorcycle operation. Hopefully, by spring, our social conscience may have a similar influence, through education, regulation, or restriction.

S. R. Maxeiner, Jr., M.D.*
Minneapolis, Minnesota

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*Minnesota Chairman of the Committee on Trauma of the American College of Surgeons.

Reference

1. Gustilo, Foss, Leslie and Telander: Motorcycle Injuries. Minnesota Med 48:489, 1965.

A psychiatrist is a man who doesn't have to worry so long as others do.
— Jacob Braude's "Speaker's Encyclopedia"

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Test Your Word Score

Watch for the asterisks in the manuscripts each month and test your word sense!

For your Word Score:

Astrotherapist — one who bases his therapy on the stars. (page 470)

Tautologic — repetitious. (page below)

Serendipity — The incidental discovery of some fact or truth not directly sought for. (page 507)

The Editor's Soliloquy

Excuse My Errors

The editing of a manuscript for the "purpose of reviewing with the idea of assessing for the value of obtaining" an appraisal of the author who wrote that gibberish is an unenviable job. Extracting and eliminating the subjective I, my, and me, and the we, our, and us from the objective background requires unlimited patience and finesse.

Those sentences which start off confidently in one direction and then get lost; those dangling participles, loose phrases, vague antecedents, confusing tenses, inaccurate abbreviations without benefit of periods; those tautologic* passages and prolix paragraphs — all can add up to literary anarchy.

In a technical thesis where precision is required, only specific, concrete terms are acceptable.

An author may speak of a large hemorrhage or a small particle, but how large is large and how small is small? One can never be quite sure whether the writer means *my* large or *his* large, *my* small or *his* small.

After reading about a short-loop gastroenterostomy with an adequate stoma, this editor consulted the next ten surgeons he met, and learned that a 'short loop' might vary from 1 cm. to 2 ft., and an 'adequate stoma' might vary from the width of the index finger to 5 cm.

Then there are those contributors who bury the value of their manuscript in a long title which in itself constitutes a short summary of the whole study; justify their work in the introduction with the substantiating authority of a few dozen investigators, providing, in addition, gratuitous and sleep-inducing monotony with a thumbnail biography of each; proceed to elaborate and detail their study in the body of the manuscript; and then 'summarize' the whole by stating in effect: I am telling you that I have already told you in the preceding paragraphs. With these pleonasms the reader is tempted to give up. The title was too cumbersome to be advantageously catalogued; the introduction was too voluminous to be read; the body of the manuscript was too embellished with redundancies to compel interest; and the summary did not synthesize in capsule form.

Even with conscientious editing, however, it is often observed, in the finished product, that the editor himself, or the printer, or an assistant has slipped up. To air is humane. — oops! — C.O.R.

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*See Test Your Word Score above.

Only presidents, editors, and people with tapeworms have the right to use the editorial "we." — Mark Twain

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Stoll[1] used the drug in 50 patients with anxiety, and noted: "There was no drowsiness in this group of patients and, because of their alertness and less impaired concentration, they were able to continue with and, in some cases, return to their daily work."

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Before prescribing, see SK&F Product Prescribing Information.

Photograph professionally posed.

1. Stoll, L. J.: The Use of Trifluoperazine ['Stelazine'] in General Practice, M. Press *243*:578 (June 29) 1960.

SK&F Smith Kline & French Laboratories, Philadelphia

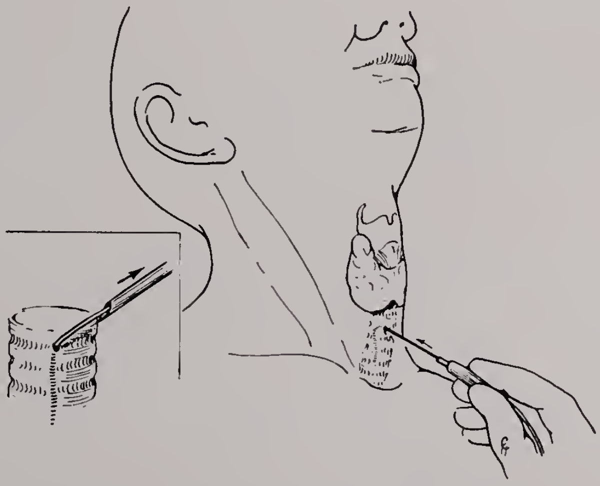
Curbstone Consultation

Bronchoscopic Irrigation

QUESTION: Do you recommend bronchoscopic irrigation and aspiration shortly after surgical operation when a patient has developed a sudden rise in temperature, and the physical examination indicates a diminished aeration?

ANSWER: Bronchoscopic irrigation and aspiration is recommended during the early postoperative period if other simpler measures have failed to improve impaired pulmonary ventilation. Bronchoscopic aspiration during the early postoperative period has not been required in my practice during the past several years since intratracheal instillation of mucolytic agents (Mucomyst, etc.) have been employed routinely to stimulate the cough reflex and liquefy mucus plugs. These instillations are given every few hours through a small transtracheal plastic tube inserted percutaneously through a needle (Intercath or Venocath) and left in place for several days.

J. Karl Poppe, M.D.
Portland, Oregon



Prevention of atelectasis by trans-tracheal injections — Northwest Medicine, June 1963.

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— Friedrich Nietzsche

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The initial response is usually maintained without dosage increases; indeed, initial dosage is often reduced for maintenance purposes.

Salicylate or steroid therapy can usually be diminished or, in some instances, eliminated.

Psoriatic arthritis responds in the same way as rheumatoid arthritis but the skin lesions are usually not affected either favorably or adversely by treatment.

Precautions
Before prescribing, the physician should obtain a complete history and perform a complete physical and laboratory examination, including a blood count.

The patient should be kept under close supervision and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools.

If coumarin-type anticoagulants are given simultaneously, the physician should watch for excessive increase in prothrombin time.

Side effects
The most common side effects are nausea, edema and drug rash. Infrequently, agranulocytosis, generalized allergic reaction, stomatitis, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug.

Contraindications
These include: edema, hypertension, or danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when other potent chemotherapeutic agents are given concurrently because of the increased possibility of toxic reactions; when the patient cannot be seen regularly; when the patient is senile.

Note: The physician should be fully aware of dosage, precautions, side effects and contraindications as contained in the complete prescribing information.

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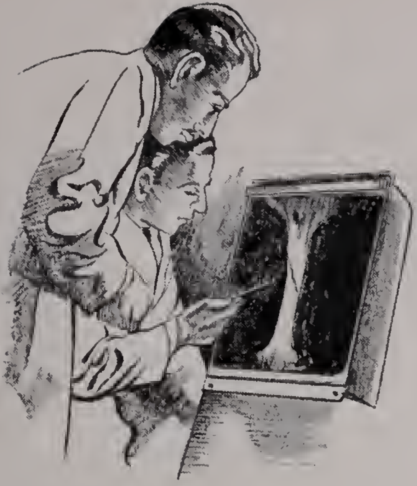

Fracture–Trauma Conference

Motorcycle Injuries

An Increasing Traffic Problem*

A distressingly large number of motorcycle accident victims have been treated in Minneapolis hospitals this summer. The recent surge in popularity of the motorcycle associated with the alarming number of injuries prompted this study.

Methods

This study is an analysis of motorcycle accidents at Hennepin County General Hospital and Methodist Hospital, covering a three-and-one-half month period from May 1 through August 15, 1964. A total of 200 accident victims were treated during this period: 121 cases at Hennepin County General Hospital and 79 cases at Methodist Hospital. The patients were first seen in the Emergency Rooms of the hospitals and evaluated. Definitive treatment was then given or the patient was transferred to another hospital of his choice. After reviewing the patient's record, each patient was sent a questionnaire inquiring as to the nature of the accident, the type of motorcycle used, the experience of the driver, etc.

Findings

Of the 79 patients seen in the Emergency Room at Methodist Hospital, 70 patients answered the questionnaire, while at the Hennepin County General Hospital, 53 of the 121 patients returned the questionnaire. Males were involved in the accidents four times as frequently as females. Twenty-four patients had been passengers on the motorcycle at the time of the accident. Ages ranged from three to 52 years, but the majority were 15 to 25 years of age (Table 1). Twenty per cent were riding the motorcycle for only the first or second time. Seventy per cent had either rented or borrowed the motorcycle (Table 2). Most of the patients seen in the suburban hospital had rented the motorcycle. All but six of the cyclists rode the light-weight motorcycles, such as Honda, Vespa, Yamaha, etc.

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*From the Hennepin County General Hospital, Minneapolis, and the Methodist Hospital, St. Louis Park, Minnesota.

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Continued

TABLE 1
Age Distribution of Motorcycle Accident Patients

	Hennepin County General Hospital	Methodist Hospital	Total
Under 10	1	1	2
11 to 15	12	9	21
16 to 20	52	37	89
21 to 25	42	14	56
26 to 30	8	3	11
Over 30	8	6	14

TABLE 2
Did You Own, Rent, or Borrow the Motorcycle?

	Own	Rent or Borrow
Hennepin County General Hospital	26	18
Methodist Hospital	19	51
Total	45	69

The exact nature of the accidents varied but could be classified into two general categories: (1) motorcycle upsets, (2) car-motorcycle collisions (Table 3). While more accidents were due to upsets, the more serious injuries occurred as a result of collisions.

TABLE 3
Nature of Accidents

1. Car-Motorcycle Collisions — 46 Cases — 38.4%
    - a) Collision with turning car.
    - b) Head-on collision with car.
    - c) Collision from rear by car.
2. Upsets From Various Causes — 79 Cases — 61.6%
    - a) Skid on road because of gravel.
    - b) Fell off for no apparent reason.
    - c) Lost control and turned over.
    - d) Accelerated too fast.
    - e) Motorcycle vs. motorcycle collision.
    - f) Unable to locate brake.
    - g) Caught fingers or feet on chains or spokes of wheel.
    - h) Hit immovable objects, post, etc.
    - I) Front wheel slipped.

The injuries were also classified as minor or major. There were 119 minor injuries and 72 major injuries in the study. Minor trauma included simple lacerations, sprains, contusions, etc., which did not require hospitalization and could be easily treated in the Emergency Room. The major category included fractures (simple, multiple, closed or open), traumatic amputations, large lacerations, cerebral contusions and intra-abdominal injuries which necessitated either hospitalization or immediate surgical intervention. Ninety per cent of the major injuries involved the lower extremities, consisting of single or multiple fractures of tibia, femur or pelvis. Two patients died as a result of their injuries; both had sustained skull fractures with brain damage.

Case Reports of Representative Injuries

Case No. 1

A 25-year-old machinist driving a Harley-Davidson motorcycle collided with a car making a left turn. The driver was thrown from the motorcycle and brought unconscious to the Emergency Room at Methodist Hospital. During the next half hour, his right pupil dilated and became fixed. Skull X rays revealed a skull fracture. At craniotomy an acute epidural hematoma was evacuated. Fractures of the left ankle, left tibia and right femur were also treated. A laceration into the left knee joint was sutured. Subsequently the patient did well and was discharged after five weeks' hospitalization with healing fractures.

Case No. 2

A 26-year-old typist riding his motorcycle home from work collided with an automobile. He arrived at General Hospital semicomatose, with a skull fracture, left femur fracture, compound left patellar fracture, left ankle fracture and compound right tibial fracture. He developed an acute abdomen which at exploratory laparotomy was found to be due to mesenteric hemorrhage. After a stormy hospital course, the patient was discharged seven weeks following admission in a spica cast with healing fractures.

The questionnaire revealed that 70% of the accident victims will not ride their motorcycles again (Table 4). Of 25 major injury cases at Methodist Hospital, only one person planned to ride a motorcycle again.

TABLE 4
Will You Ride the Motorcycle Again After the Accident?

	Yes	No
Hennepin County General Hospjital	22 — 41.6%	31 — 58.5%
Methodist Hospital	16 — 23.0%	54 — 72.0%
Total	38 — 30.9%	85 — 69.1%

Discussion and Conclusions

The public should be apprised of the hazards of operating motorcycles. The number of accidents due to upset of the machine points to the fact that it is basically an unstable vehicle. The popular light-weight machines are most frequently involved in accidents, a fact which may well be due to the inexperience of the driver as well as to the excessive speed and power of these machines in relation to their weight. Many patients commented that the rental agency involved provided inadequate instructions and orientation in the operation of the machine, and it would seem appropriate that some measures of control should be exercised in this regard.

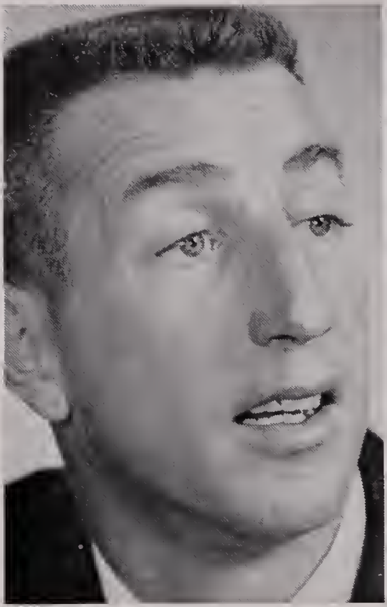
Many accidents can be classed as the "low-speed type" where major injuries are sustained because the driver has little bodily protection on the motorcycle. Frequently motorcycle accidents occur because the driver of the automobile did not see the motorcycle. Some have resulted when the motorcycle was passing a car on the right side as the car made a right turn.

Fatalities from skull fractures and head injuries could probably be reduced by use of a protective helmet. There is no protection, however, to be applied for the extremities. The high incidence of arm and leg fractures in this study attests to the serious exposure of the cyclist to crushing forces. It would be prudent to insist that drivers of motorcycles receive special instruction and demonstrate proficiency in the use of these machines before venturing onto our highways and city streets.

Ramon B. Gustilo, M.D.**
Donald L. Foss, M.D.
William R. Leslie, M.D.**
Robert L. Telander, M.D.
Minneapolis, Minnesota

**St. Louis Park Medical Center, Minneapolis, Minnesota.

Man is not the creature of circumstances. Circumstances are the creatures of men.
— Disraeli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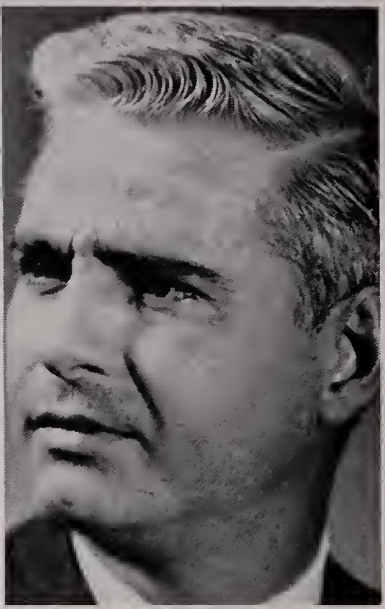
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Tumor Conference

Follicular Adenocarcinoma of Thyroid Gland

A lady, age 40, was admitted to Hennepin County General Hospital, having been seen in the E.N.T. Clinic with a complaint of stuffiness in the nose. At this time it was noted that she had an enlargement in the right side of the neck which appeared to include the right thyroid and lymph nodes, with a normal gland on the left side. A compete E.N.T. examination revealed nothing that could be considered a source of the enlarged nodes, either inflammatory or neoplastic, from within the nasopharynx itself.

The past history included an appendectomy at age 14 and a complete abdominal hysterectomy in 1962. There was no history of any medical disorders.

Physical Examination

The physical examination noted three palpable half to one-centimeter nodes in the right neck, located along the anterior border of the right sternocleidomastoid muscle. The right thyroid gland was firm and slightly enlarged and fixed to the trachea. While the patient was in the hospital, a repeat E.N.T. examination, including tonsillar biopsies, was done. Laboratory data included radioactive iodine uptake of 13.6% in 24 hours with a dose of 50 mc. of I 131, a PBI of 3.6 gamma per cent. Normal urine and hemoglobin of 13.9 grams; normal WBC and differential; pulse and blood pressure normal 80 and 110/76. A thyroid scan was done, showing no uptake in the right lobe and an essentially normal configuration of the left lobe, with the possibility of a toxic nodule.

Operation

A total right lobectomy, including the isthmus and approximately one half of the left lobe, was done with adjacent strap muscles and a right radical neck dissection, including the internal jugular and sternocleidomastoid muscle. The recurrent laryngeal nerve was preserved.

At the outset of the operation, upon exposure of the node-bearing area, one lymph node adjacent to the inferior portion of the right thyroid lobe was sent for frozen section. This appeared to be normal thyroid with some papillary appearance. After the specimen was removed, another frozen

Continued

section of the gland itself revealed a well differentiated carcinoma of the thyroid.

Pathological Report

Eleven of the twelve lymph nodes examined contained follicular structures. The thyroid tissue showed hyperplastic follicular elements generally filled with deep eosinophilic-staining colloid material. The cells of the glandular spaces were low cuboidal. There were areas of fibrosis as well as areas in which the glandular spaces contained no colloid, thus giving some distinct papillary appearance with large pale-staining cells and other small round follicles with no colloid. Approximately one half of the nodules contained definite lymph-node structure. The tail of the parotid gland contained no tumor.
Diagnosis: Follicular adenocarcinoma of thyroid gland with extension to lymph nodes.

Discussion of the Problem

A recommendation for future management and therapy is sought, with the following questions being posed:

1. In the absence of definite involvement or extension into the left lobe, should the remainder of it be removed or ablated on the possibility of future radioactive iodine uptake by metastases?
2. In case of local recurrence or distant metastases, what type of management would be recommended?

James Bascom, M.D.
Chief Surgical Resident
Lee Simso, M.D.
Surgical Resident
Hennepin County General Hospital

Commentary by Dr. Irving M. Ariel

Dr. Ariel was present at the Tumor Conference presentation of this case and has been kind enough to review his opinion. He had come to Minneapolis in November, 1964, to present a lecture to the Minneapolis Surgical Society, and another on the following day to the Minnesota Surgical Society. Dr. Ariel and Dr. Pack are coauthors of 12 recent volumes on cancer.

"I would consider this case a follicular cancer and treat it as such. The presence of the papillary elements would not influence my over-all approach. Follicular cancer comprises only between 10 to 15 per cent of all thyroid cancers, and metastases to lymph nodes are seen in about 30 per cent of patients when they first present themselves for treatment. This tumor is particularly prone to develop blood-borne metastases which will be found in approximately 45 per cent of patients. The five-year survival or even cure rate is about 66 per cent. In view of these data, I would believe that the right thyroidectomy and neck dissection are sufficient, and I would not be inclined to give any further therapy.

It seems to me that there was some mention that involvement was found in the opposite lobe and that this was treated by hemithyroidectomy. Here again, even though a conservative procedure was done for cancer involving a given lobe of the thyroid gland, it would be my reaction to do nothing but watch further developments. I believe that the patient has a good chance for cure.

However, if one were inclined to do something, and in view of the avidity of follicular cancer for radioactive iodine, one may very readily give a course of radioactive iodine to this patient. My own personal preference would be not to do so, even though I recall that in the discussion I did state that I would. This is simply a matter of personal preference, rather than an out-and-out standard for treatment practice. If one should decide to give the radioactive iodine, it would be a safe way of destroying any residual cancer within the gland. Rather than give a massive dose as some therapists do, it has been my policy to give between 20 and 30 millicuries about every two to three months until the patient has been rendered completely hypothyroid, at which point I give Cytomel. This course of therapy would also have the added advantage of treating any cryptic metastases which may exist. I would not resort to any further surgery.

The reason I would not be inclined to do anything is due to a lesson which I learned from George Pack many years ago to the effect: "Treat cancer where you find it." In view of the fact that you don't know whether or not you have cancer in the opposite lobe, you are treating a statistic. Furthermore, I'd like to know exactly what I am treating. Therefore, I would be inclined to subject this patient to a radioactive iodine scan every so often, scanning not only the thyroid region, but also the cervical region, as well as the lung and bone regions for possible metastases to other sites. Should these occur, then you will be armed with the knowledge of the nature of the particular tumor and treat it accordingly.

In case of recurrence, I would again treat this patient exactly as I would any cancer patient, sticking strictly to cancer tenet treatments. If a recurrence developed on the left side, I would then go ahead and perform a left thyroidectomy and radical neck dissection, as you did for the opposite side. This, of course, is contingent on the fact that there are no other metastases present elsewhere. If metastases are present, then I would be inclined to be guided by their extent and nature. If they are widespread, I would be conservative and inclined to depend upon a course of radioactive iodine therapy. If the local recurrence did not respond, then I would conservatively resect them. If they existed in the thyroid gland alone, I would remove the gland; if the patient had lymph nodes containing metastases, I would then do the neck dissection.

In my scanning, I would also include the brain, as this has been a frequent site of metastases in my experience.

I hope I have not been too confusing. I have tried to relate the standards of treatment as well as to interject my own personal beliefs and practices."

Irving M. Ariel, M.D.
Pack Medical Group
New York, New York

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*Chupkovich, V.; Finnerty, F. A., Jr., and Kakaviatos, N.: The value of chlorthalidone plus reserpine in moderately severe and severe hypertension: A two year study. Presented at the 7th Inter-American Congress of Cardiology, Montreal June 14–19, 1964.

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Neurological Conference

Herpes Zoster*

Today we are considering a case of herpes zoster in a man 58 years of age. Although the inflammatory involvement has been limited to his left face and eye, the degree of incapacitation has been great. Not only has he had to cease gainful employment, but he has been extremely uncomfortable because of severe pain. Beyond that, totally satisfactory recovery is still in doubt.

Dr. Robert Anderson**

The patient, who is 58 years old, had been in good health until July 10, 1964, when he developed a "pins-and-needles" feeling in the left side of his scalp. This unusual tingling persisted night and day for about one week before watery blisters appeared over the distribution of the ophthalmic division of the fifth cranial nerve. Hospitalization became necessary because of the severe pain in this area; there was also an inflammatory breakdown of the skin with weeping and crusting of lesions. Darvon Compound was used to control the pain, and occasionally thorazine was used to quiet the patient. Moist boric-acid packs were applied to the face. During this time he also developed a scratchy feeling in the left eye and blurred vision. Subsequently he was referred to the University of Minnesota Medical Center for the complicating eye involvement and persistent pain. Examination at the time of his visit to New Medicine Clinic revealed a pustular, crusting erythematous dermatitis of the left face, characteristically ending at the mid-line involving half his nose and extending into the left scalp. The conjunctiva of the left eye was markedly injected; the left cornea was clouded, and the pupillary light reflex on the left was reduced. The involved skin was hyperesthetic to stimulation.

There had been no exposure to chicken pox, although there may have been to shingles.

Dr. Richard Meyer†

The patient was admitted to the local hospital with severe keratitis and dermatitis over the distribution of the left fifth nerve. In the hospital his

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*Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatric conferences are held the first and third Wednesdays of every month from 3:15 to 4:15 p.m. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Robert W. ten Bensel, in Pediatrics, and Dr. Robert Soll, in Adult Neurology.

**Student doctor, University of Minnesota Medical Center.

†Family physician from Faribault.

eye was treated with ophthalmic ointments. Some relief was obtained but he still had a tremendous amount of reaction in the skin area over his left temple, much like a second degree burn. Weeping of the skin gradually ceased and his pain eventually moderated, although he continued to have typical attacks of sharp pain, which were intermittent and of short duration. We discharged him on September 12, after nine weeks' hospitalization, at which time he was relatively free of pain. After a week, however, the pain again became more severe and the conjunctivitis and keratitis worsened.

The pain that he had prior to his admission to this hospital was not as severe as the pain that he had had at the onset of his illness. It was considerably worse, however, than he had had at the time of his discharge from the local hospital.

There had been no evidence of a hearing impairment, but there were several episodes of what seemed to be a psychotic reaction during the last two or three weeks of his hospitalization. These episodes occurred intermittently, perhaps twice a week, and each lasted about six hours. He was given thorazine, 50 mg., intramuscularly every four to six hours. After sleeping four to six hours, he would awaken, appearing much improved. His wife called me about two weeks ago, after he had again become excited, irrational, and unable to recognize a number of his friends. He also became belligerent during this time. This episode lasted over two days and constituted quite an unusual departure from his ordinarily withdrawn behavior. There was never any amnesia associated with this unusual behavior.

Neo-cortone ointment, a combination of a steroid and neomycin, as well as neo-polycin ointment, which does not contain a steroid, were used.

Dr. Raymond Gingrich*

The patient had a typical herpes keratitis as well as inflammation of the uveal tract. His vision was only 20/400 in the left eye.

In the usual case of ophthalmic herpes zoster numerous white blood cells accumulate in the anterior chamber of the eye. Small blisters then develop over the cornea and eventually rupture. Concomitantly the cornea becomes over-hydrated and very painful, and vision is considerably decreased. Therapy is directed towards (1) reducing the inflammation, (2) dehydrating the cornea, and (3) preventing any sequelae of the inflammation itself. Steroids are very important for accomplishing these goals. Treatment of herpes zoster is different from treatment of herpes simplex. In the latter, they have isolated the virus directly from the vesicular lesions. Consequently, steroids are not used in herpes simplex in the early stage since further growth of virus may be encouraged. On the other hand, iododeoxyuridine, which is a deoxyribonucleic-acid analog, has been tried in herpes simplex with some success. The virus readily accepts this analog, which in turn prevents the virus from duplicating itself. This is probably the first drug that has been found to work effectively against the virus. Because of the inhibitory action of iododeoxyuridine, its use could permit the simultaneous employment of steroids in late herpes simplex. Otherwise, the use of steroids in herpes simplex is contraindicated because the cornea may perforate. Herpes zoster, on the other hand has not been shown to have any virus in the corneal lesions.

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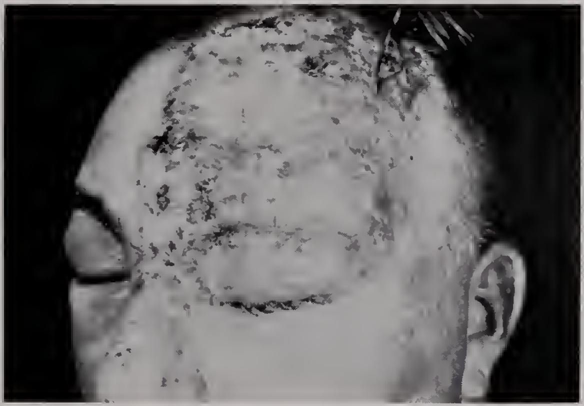
*Fellow, Department of Ophthalmology, University of Minnesota Medical Center.

Possibly the damage of herpes zoster may be a neurotrophic type due to an interruption of the nervous innervation. The cornea simply seems to degenerate much the same as the atrophy of muscle when a motor nerve has been severed, and a corneal ulcer may form.

We use cortico-steroids, both systemically and topically, to reduce the inflammation. Atropine solution is used locally to keep the pupil dilated, thus preventing adhesions between the lens and iris. The formation of adhesions could result in a complicating glaucoma by obstructing the outflow of aqueous humor. A dehydrating agent such as a 5% solution of cellulose gum can be used to remove excess fluid from the cornea. A protective shield may be placed over the eye to prevent external traumatic damage. Topical ophthalmic ointments are frequently used to prevent a secondary bacterial infection. All we can hope to accomplish is to reduce the severity of involvement and trust that the patients will improve by themselves.

ACTH could be used to advantage if an elevated steroid level could be maintained. Its use is somewhat controversial in our department. The concomitant use of ACTH with the cortico-steroids would help prevent atrophy of the adrenals.

The aseptic accumulation of white blood cells in the anterior chamber of the eye could have an allergic origin. Certainly herpes simplex is strictly a viral infection initially, but in a secondary reinfection of simplex there are deep plate-like lesions; this probably indicates hypersensitivity.



Herpes zoster of the ophthalmic division of the fifth cranial nerve.

Dr. John Brantner*

We had considerable difficulty with the psychological testing, mainly because it took more than one interview to complete the examination. The patient required hours to finish the multiphasic (MMPI). Basically he is a pleasant man to talk to, and one gets along comfortably with him. A curious aspect about him and his family is their frank acceptance of this unusual illness. His wife and son co-operate with him and try to do whatever they can, not becoming overly alarmed. My impression of the family is that they are calm, stable people. The patient has an IQ of about 80. I suspect that much of the family's apparent stability and strength could be partly due to an unawareness of the serious problems involved.

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*Clinical psychologist, University of Minnesota Medical Center.

Continued

The patient himself is confident and hopeful. On minimal testing for organic brain damage there is a strong indication of some central involvement; however, I am not sure that this is related to his disease. He also shows pretty clear evidence of a psychotic-like adjustment. I cannot determine whether this is an organic or functional psychosis. In talking to him we have no definite clues concerning this; yet he described one hallucination which was perfectly vivid to him and lasted a couple of days. In it he saw a neighbor using several white horses, razing barns and wrecking his property. When the patient came out of this he was extremely startled to find that all the destruction that he thought he had observed had not actually occurred. His son and his wife understand and believe these episodes are due to his illness; they accept them and do what they can.

On the multiphasic the patient shows a psychotic pattern that does not occur frequently in either psychiatric or medical cases. In the medical cases it is associated with borderline psychoses with elements of withdrawal, anger, and hostility. There may be short periods of confusion, disorientation, and a characteristic apathy, shown by a willingness just to drift along. Frequently associated with this is a concern over physical health, although the physical complaints the patient refers to in the multiphasic certainly seem to be referable to his present disorder. From what Dr. Meyer stated, there may have been episodes of hallucinations prior to this illness, and we may be dealing basically with a border-line psychotic. There are some signs of organic brain damage, clear evidence of psychotic behavior, a multiphasic revealing a border-line psychosis, and evidence of limited intellectual ability.

Dr. Soll

This is interesting from the point of view that cerebral involvement may complicate herpes zoster. Seizures have been known to occur, and with this in mind we obtained an electroencephalogram; however, it was normal. The patient has potentially serious family problems regarding his work status. Would you tell us the results of your interview with the patient, Miss Kretchmer?

Miss Helen Kretchmer*

I interviewed the patient and his wife as a couple. They apparently present themselves as a couple wherever they go. She has accompanied the patient to every appointment since he has been coming to the University Hospitals.

The patient and his wife seem to be pretty close, since a question posed to one produced a response from both. During the interviews they were relatively passive, accepting individuals, at least superficially. They seem to enjoy each other and also the social aspects of their hospital contacts. The patient was very receptive to medical care here and had almost a mystic attitude toward his illness, relating it to his past illnesses and surgery. He feels that he has had a difficult time, but is confident that he will recover completely. He is currently on a six-month leave of absence from work, terminating some time in January, 1965, and he plans to be well by that time. His primary concern about the pain in his left eye seems to be reduced to a great extent, and his outlook seems to be quite cheerful now.

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*Supervisor and assistant professor of social service, University of Minnesota Medical Center.

The patient went through elementary school, completing the sixth grade. The army rejected him twice because of a hernia, poor feet, and poor eyesight on the left. He and his wife were married when he was 22 and she was 21. They live in their own home, a duplex, which they value at about $8,000. I am giving a little detail on the financial situation, because I think there has been some concern about how they are going to manage until he returns to work. They have about $200 left to pay on the duplex on the basis of $10 a month. They rent an apartment at $15 a month to tenants who do all maintenance of the apartment. A son, aged 19, drives a truck and snow plow for the State Highway Department. The patient's mother-in-law, aged 90, also lives with them. She has had a stroke and was recently ill with "shingles." She is able to get around and loves to wash dishes, which the patient's wife allows her to do. Her income is $60.70 a month from Old Age Assistance. So they have little bits of income from various sources. Before the patient became ill he used to plow gardens. Actually their present income is limited to $100 a month from insurance carried by the company, although they don't know how long this will continue. The patient has worked 20 out of the past 26 years at one company, operating a carding machine, working in a warehouse, and most recently stocking, grading, and maintaining records. He is quite proud of having acquired a more responsible position. His income normally is about $60 a week and he expects to be eligible for social security at age 65. Their savings, about $600 from a former company pension, equals his local hospital bill. They had hoped to buy a furnace with that money, but now will be unable to do so. The patient does have some hospital insurance, supplemented by county authorization. Thus, since their needs are modest, I feel they are not really insecure. If he were not able to return to work in January, 1965, there might be a possibility of assistance from local agencies such as Aid to the Disabled, or from the welfare board. If he were permanently disabled, social security disablement could be considered.

Dr. Soll

From the neurological point of view, these are extremely difficult problems to treat. Herpes zoster, whether it be cranial-nerve or spinal-nerve involvement, almost invariably produces severe pain, sometimes even after the superficial skin lesions actually heal. During the acute phase, calamine lotion may be applied to the superficial lesions to promote soothing and drying. If the lesions are unruptured, collodion may be applied to prevent their breakdown. The pain is much more difficult to treat. Aspirin and codeine often afford relief, but sometimes more potent narcotics may be required. However, prolonged use of narcotics should be avoided. Often the use of deep X-ray irradiation to the nerve roots or trigeminal ganglion will alleviate the pain, but it should not be used during the acute phase of the disease. It is possible to approach the problem of persistent, unrelenting pain surgically if the zoster is of spinal origin. Section of the lateral spinothalamic tract above the level of the lesion can afford relief. Such a procedure cannot be done, however, when the cranial nerves are involved. ACTH or other cortico-steroids such as decamethasone during

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the acute phase may prevent the postherpetic complications by reducing the inflammatory reaction.

Elderly people are frequently more debilitated by herpes zoster than younger individuals. The virus of herpes zoster is thought to be the same as the virus causing chickenpox. Cases have been reported in which herpes zoster and chickenpox have occurred simultaneously in different members of the same family, the children usually having chickenpox. This may mean that people who lose their immunity to varicella may become susceptible to herpes zoster as adults.

I think it would be interesting to ask the patient directly what his outlook is about getting back to work.

Dr. Soll: Do you recall, was your pain initially the same kind of pain as it is now?

Patient: It is the same kind of pain but not as bad.

Dr. Soll: Do you have a lot of trouble seeing?

Patient: Yes, I have trouble even seeing television. I usually sleep or listen to the radio.

Dr. Graham Beaumont:* How many pain pills are you taking each day?

Patient: About three or four.

Dr. Beaumont: Does the pain wake you at night?

Patient: That's the funny thing — I have good nights, but it begins to hurt again after I wake up.

Dr. Beaumont: What sort of work do you do?

Patient: I have to do some reading, weighing things — a lot of the work is pretty close up.

Dr. Soll

In summary, this 58-year-old patient has been incapacitated by herpes zoster involving the ophthalmic division of the left fifth cranial nerve for the past three and one-half months. The chief complications have been persistent pain and a severe ophthalmic keratitis which has markedly reduced the vision in his left eye. Non-narcotic analgesics have controlled the pain fairly well. Cortico-steroids are being used locally and systemically to control the keratitis of the left eye. Psychologically there is suggestive evidence of organic brain involvement. The social-service interview reveals that the financial status is meager but probably adequate for the time being. The patient's capability of returning to work will depend greatly on his response to treatment in the next few weeks; this response, in turn, will determine what further efforts will need to be done both medically and by social welfare.

Robert Soll, M.D.
University of Minnesota
Medical Center

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*Director of Medical Admissions, Clinic, University of Minnesota Medical Center.

Participating in the conference was the patient's family physician, Dr. Richard Meyer. The following participants are from the University of Minnesota Medical Center: Robert Anderson, Student Doctor; Dr. John Brantner, Clinical Psychologist; Miss Helen Kretchmer, Supervisor and Assistant Professor of Social Service; Dr. Graham Beaumont, Director of Medical Admission's Clinic; Dr. Raymond Gingrich, Fellow, Department of Ophthalmology; and Dr. Robert Soll, Chairman, Adult Community Services.

Reference

Elliot, F. A.: Treatment of Herpes Zoster with High Doses of Prednisone. Lancet 7360: 607, 1964.

Advances

Infections of the Urinary Tract

Part IV. Antibacterial Regimens*

WILLIAM J. MARTIN, M.D.**
RICHARD D. WAGONER, M.D.**
Rochester, Minnesota

IN THE management of infections of the urinary tract, the individual situation may influence selection of the drug to be used; vomiting may disallow use of usual therapy if that therapy ordinarily is given orally. Previous allergic reactions or current intolerance of an agent may disqualify it for use.

Renal insufficiency makes mandatory the careful use of certain drugs that are either nephrotoxic or potentially toxic to other organ systems. When resistant organisms are encountered, the intrinsic severity of the infection is the keystone to deciding whether the risk associated with the use of more toxic antimicrobial agents is justified.

Acute Simple Infection

Since acute simple infections are common, may be transient, and seldom require heroic therapy, treatment may be initiated after preliminary identification of the bacteria by the examination of a stained preparation of the urinary specimen. In this regard, acute uncomplicated infections often have appeared to subside without specific treatment. Failure to eradicate the infection requires further study, including urologic and microbiologic, to exclude predisposing disease, an underlying lesion, resistant organisms, and so forth.

As a general rule, bacteriostatic agents, including those that are not antibiotics, are used in acute simple infections. For the more serious or complicated infections, bactericidal agents may be preferable, with consideration of the usual limitations of drug toxicity and routes of administration. Nonantibiotic antibacterial agents currently used in the therapy of acute simple urinary infections include (1) the sulfonamides, (2) nitrofurantoin (Furadantin), (3) nalidixic acid (NegGram),[19] (4) methenamine mandelate (Mandelamine), and (5) acidifying agents such as methionine.

If the physician is convinced that there is an acute, uncomplicated urinary infection, he may wish to use a sulfonamide because of its low cost and ease of administration. Sulfonamides may be given in amounts of 0.5 to 1 gm., four times daily. In other patients, such as those allergic to sulfonamides, nitrofurantoin in amounts of 50 to 100 mg., four times daily, may be preferred. In some of these latter patients who have infection due to coli-aerogenes or Proteus organisms, nalidixic acid may be elected in amounts of 0.5 to 1 gm., four times daily by the oral route. In certain infections, especially enterococcal, methenamine mandelate may be used in amounts of 0.5 to 2 gm., three or four times daily. The mandelic acid component of methenamine mandelate helps acidify the urine, releasing formaldehyde from methenamine. The formaldehyde is antibacterial to both gram-negative and gram-positive organisms, and bacterial resistance probably is not a problem. However, despite the mandelic acid component, supplemental acidification may be required, particularly with urea-splitting organisms.

Decrease of urinary pH and of bacterial

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*See Part I, Minnesota Med., January issue, Page 95, Part II, February issue, Page 231, Part III, March issue, Page 379.

**Section of Medicine, Mayo Clinic and Mayo Foundation.

counts in the urine may follow the use of 8 to 15 gm. of methionine daily; however, when more than 8 gm. is given per day, the patient may complain of the odor of hydrogen sulfide about his person. The sulfur in methionine is oxidized to sulfate and is excreted in the urine, making it acid. Other acidifying agents such as ammonium chloride, ammonium mandelate, calcium mandelate, and ascorbic acid have been given in conjunction with methionine; if urinary pH can be reduced to 5 or less, the desired antibacterial effect may be procured, but it is difficult to maintain the desired pH without inducing metabolic acidosis. In short, the physician may avoid giving more than 8 gm. of methionine daily by using in addition another agent such as ammonium chloride, so as to decrease the likelihood of inducing the odor of hydrogen sulfide. Also metabolic acidosis may be avoided by giving, in addition to the acidifying agents, methenamine mandelate. Use of an acid-ash diet or of hippuric acid (which is present in cranberry juice) are not currently in common use. When attempts are made to keep the urine acid, the physician considers restricting the patient's fluid intake to 1200 ml. a day and the avoidance of foods, primarily citrus fruits, and drugs, such as sodium bicarbonate and milk of magnesia, which increase the alkalinity of the urine. Also, the patient should periodically determine, by means of nitrazine paper, whether his urine is properly acidic.

Recurrent Infection

Nonantibiotic antibacterial agents may also be used when extensive investigation is unrewarding and yet infection continues to recur; 0.5 gm. of a sulfonamide, 50 to 100 mg. of nitrofurantoin or 0.5 to 1 gm. of nalidixic acid is given two to four times daily for five to 10 days monthly for several months. Such a procedure may serve to prevent further recurrences.

Recurrent infection in the absence of demonstrable underlying uropathy or predisposing disease may not necessarily represent a series of unconnected and isolated episodes. Rather, the exacerbations may represent reactivation of temporarily quiescent bacteria that have continued to dwell in the urinary tract. However, while definitive knowledge is lacking, repeated episodes of infection probably reflect reinfection, relapse, and superinfection in decreasing order of incidence. Micro-obstructive changes within the nephron due to prior infection may enhance the possibility of future infection. Recurrences of infection are usually due to reinfection with new strains presumably from the fecal flora contaminating the perineum. Antibacterial prophylaxis may provide an infection-free interval during which the patient's tissues may develop greater resistance to potential infection in the future. Attempts at antibacterial prophylaxis are usually made for at least six months following control of the preceding infection; after this time, prophylaxis may be discontinued in the hope that further medication will not be required.

Chronic Infection

The nonantibiotic agents, except possibly nitrofurantoin, may also have application in certain chronic infections in which underlying uropathy is uncorrectable or more heroic therapy has proved ineffective. Intermittent or continuous administration of these agents in such cases may minimize the patient's symptoms, and in some cases sterilization of the urine ultimately is achieved. In patients with chronic infection, suppressive therapy may be continued indefinitely, especially if exacerbations are thereby lessened, in the hope that the degree of progressive renal damage is being reduced. In these latter patients, such therapy more often is intermittent; for example, it is given the first week of each month or every other week rather than continuously. Use of nitrofurantoin in some of these patients is avoided because therapy is prolonged and decreased renal function is common; both of these factors might enhance the likelihood of nitrofuran neuropathy.[20] In this regard, the manufacturer of nalidixic acid recommends that the drug be given cautiously in patients with renal impairment. Also, methenamine mandelate should not be given to patients with renal insufficiency. Even use of the acidifying agents in the presence of renal insufficiency is not without hazard.

Persistence of infection in this group appears to be more often related to the structural and physiologic abnormalities of the urinary tract than to the drug employed. Thus, the pertinence of an antibacterial regimen is not well evaluated on the basis of its ability to render the urine permanently sterile.

Severe Infection

Often in more serious urinary infections, other agents must be used. Severe urinary infections mean those that are characterized by a violent systemic reaction, those that persist after recent surgical correction of underlying uropathy, those in which renal function appears to be seriously threatened, abscesses, and the like.

Severe Gram-Negative Bacillary Infection

Up to the present, combined streptomycin-tetracycline therapy has been preferred in serious infections due to gram-negative bacilli prior to report of sensitivity tests. Use of ampicillin or cephalothin in infections due to E. coli; ampicillin, cephalothin, novobiocin, or penicillin in infections due to Proteus mirabilis; cephalothin in Proteus infections including those due to the mirabilis strain; polymyxin B or sodium colistimethate (Coly-Mycin injectable) in Pseudomonas infection; and chloramphenicol, cephalothin, or ampicillin in Salmonella infections may be considered if the patient's course and in vitro susceptibility tests so indicate. The newer antibiotic, sodium colistimethate, although less efficient weight for weight than polymyxin B, is also described as being less toxic; but this is disputed.

Streptomycin-tetracycline treatment given empirically for serious infections due to gram-negative bacilli has been preferred for several reasons. The onset of bacterial resistance may be delayed by the use of multiple antibiotics and enhanced effect obtained; and when such treatment is given before susceptibility tests are reported, broader antibiotic coverage is provided. Also, there may be discrepancies between bacterial susceptibility as determined by in vitro tests and that observed clinically involving one or both drugs.

In infections due to gram-negative bacilli not responding to tetracycline-streptomycin, susceptibility tests to chloramphenicol and kanamycin also may be procured with a view of substituting one or both agents. Chloramphenicol-kanamycin is not used routinely in the empiric management of gram-negative bacillary infection because these agents have greater potential toxicity than tetracycline-streptomycin. Also rarely, polymyxin B or sodium colistimethate is used in gram-negative bacillary infections other than those due to Pseudomonas organisms if the infections are not responding readily to streptomycin-tetracycline therapy.

Disadvantages accruing to the empiric use of tetracycline-streptomycin therapy are possible; but these are also possible with alternative antibacterial agents. The disadvantages include the dual depressive effect on the gram-negative elements of the flora, making coccal superinfection more likely. Streptomycin, kanamycin, and polymyxin B are nephrotoxic; streptomycin and kanamycin also are ototoxic, and polymyxin B may cause cerebellar ataxia. Periodic study of smears and cultures of the sputum and stools during antibacterial therapy may reveal change in the flora and impending superinfection.

Ampicillin, the semisynthetic orally administered agent, appears to have use in infections due to strains of E. coli, Salmonella, and Proteus.[19] The drug is ineffective against Pseudomonas and Klebsiella organisms. Although active against gram-positive cocci, it is less so than penicillin G and is ineffective against penicillin G-resistant staphylococci.

Cephalothin, a semisynthetic derivative of cephalosporin C is given intramuscularly.[19] Cephalothin resembles ampicillin in that it is active against strains of gram-negative bacilli and gram-positive cocci, and in addition against penicillin G-resistant staphylococci. It is ineffective against pseudomonades and some enterococci.

Gentamycin is another drug being investigated.[19] It resembles neomycin and kana-

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mycin in its antibacterial spectrum and toxicity but may be more effective against Pseudomonas organisms than either neomycin or kanamycin.

Severe Streptococcal Infection

Combined penicillin-streptomycin therapy is indicated for serious infections due to enterococci, for example, Str. faecalis. Infections due to other strains of streptococci such as Str. pyogenes and viridans may respond to treatment with penicillin alone. In persons allergic to penicillin, erythromycin is the drug of choice.

Severe Staphylococcal Infection

The treatment of staphylococcal infections depends largely on results of bacterial susceptibility tests. If staphylococci are sensitive to penicillins G and V, these remain the drugs of choice; in mild infection, orally administered penicillin V has been successful. Potassium phenethicillin (Syncillin, Darcil) and penicillin V can be used interchangeably. There is cross-resistance among penicillins G and V and phenethicillin.

Among the commercially available antistaphylococcal semisynthetic penicillins there are sodium methicillin (Staphcillin), which must be given parenterally, in addition to sodium oxacillin (Prostaphlin) and nafcillin (Unipen), which can be given either orally or parenterally. These drugs retain their antibacterial activity in the presence of staphylococcal penicillinase and hence remain effective against staphylococci resistant to other penicillins. However, none of them is automatically the drug of choice in all urinary infections due to staphylococci resisting other penicillins. This is so because other effective, orally absorbable, and less toxic antibiotics are available, and because of the physician's desire to limit the use of the semisynthetic antistaphylococcal penicillins so as to minimize staphylococcal resistance to them. Unfortunately there is cross allergenicity among these agents and the other penicillins.

Generally, erythromycin is used when the organism is sensitive to it and resistant to penicillins G and V or when the patient is allergic to penicillin, since erythromycin can be given orally and is virtually nontoxic. When staphylococci resist erythromycin, lincomycin might be considered since it is orally absorbed. Use of the propionyl ester of erythromycin and triacetyloleandomycin is often avoided in the treatment of infections of the urinary tract because control of the process may require two weeks or longer and the drugs given for such periods may prove hepatotoxic.

Lincomycin is said to be bactericidal, but it may be hepatotoxic and perhaps hematotoxic. All staphylococci do not appear to be sensitive to its action. Thereafter, use of novobiocin might be considered.

If erythromycin, lincomycin, or novobiocin cannot be used, then a semisynthetic antistaphylococcal penicillin may be the drug of choice. If such a drug is not applicable as in patients who have previously exhibited allergy to penicillin, cephalothin may be tried. Although both kanamycin and vancomycin are toxic to the eighth cranial nerve, kanamycin may be considered before vancomycin, since kanamycin is given intramuscularly and vancomycin must be given intravenously. Chloramphenicol follows vancomycin in the list of selections, even though it has the advantage of being orally absorbable, because of its propensity to depress the marrow, and it is considered before ristocetin, which can also depress the marrow but which has the added disadvantage of requiring intravenous administration. Before or after consideration of chloramphenicol and ristocetin, depending on the fear of ill effects on the marrow as well as on the laboratory facilities available, combined antibiotic therapy can be considered. In attempts at combined therapy, however, the staphylococcus organisms should be susceptible on in vitro testing to both agents used. In such therapy a bacteriostatic agent such as erythromycin, novobiocin, or chloramphenicol might be employed with such bactericidal agents as bacitracin or neomycin.

The physician hesitates to use the tetracyclines in hospitalized patients because of the superimposed infections with resistant organisms that may ensue. Streptomycin has limited application as an antistaphylococcal agent, since staphylococci rapidly develop resistance to it. Polymyxin B, colistin, the sulfonamides, nitrofurantoin, nalidixic acid, methenamine mandelate and acidifying agents such as methionine have virtually no application in the treatment of serious staphylococcal infections.

When severe staphylococcal urinary infections demand treatment before the results of susceptibility tests are available, an agent can be given that previous experience has shown the staphylococci will most likely not resist. Methicillin or an allied drug, cephalothin, or vancomycin might be selected, and after 24 to 48 hours, when the results of susceptibility tests are known, the physician may be able to substitute a more pertinent or less toxic antibiotic.

Other semisynthetic antistaphylococcal penicillins under investigation are cloxacillin, dicloxacillin and diphenicillin. Cloxacillin on oral administration gives higher serum levels than oxacillin. Dicloxacillin gives levels twice as high as cloxacillin and four times as high as oxacillin. Diphenicillin also can be given orally and has been said to compare favorably with oxacillin.[19] Sodium fusidate also diphenicillin is being investigated as an antistaphylococcal agent.[19]

Severe Polymicrobic Infection

In serious infections due to multiple organisms, several drugs may have to be given simultaneously. The physician might give penicillin along with streptomycin in infections with Str. faecalis and simultaneously give a tetracycline to combat E. coli. Since it is difficult to say which organism is most important in such infections, broad coverage is necessary since estimation of the infectious capabilities of the individual organisms may be erroneous. Ampicillin may have special use in polymicrobic infections; cephalothin also warrants consideration in this regard.

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Two Cases of Serendipity*

In the biological sciences serendipity has been quite as consequential as in the physical sciences.

Pasteur was led by chance to his method of immunization. One day an old and forgotten bacterial culture was being used for inoculating fowls. The fowls became ill but did not die. This happening was illuminative. Possibly by first using cultures that had little virulence and then repeating the injections with cultures of greater virulence, the animals could be made to develop resistance to infection gradually. His surmise proved correct.

In the late eighties of the last century, von Mering and Minkowski were studying the functions of the pancreas in digestion. While attempting to secure more evidence they removed that organ from a number of dogs. By good luck a laboratory assistant noticed that swarms of flies gathered round the urine of these animals, a fact which he mentioned to the investigators. When the urine was analyzed, it was found to be loaded with sugar. Thus for the first time experimental diabetes was produced, and the earliest glimpse was given into a possible cause of that disease. (Walter B. Cannon)**

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*See Test Your Word Score, Page 485.

**Rapport, Samuel, and Wright, Helen: Great Adventures in Medicine. The Dial Press, New York, 1952, p. 519.

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Grand Rounds

Salicylate Intoxication

Though many new pharmacologic products have been made available, salicylates continue to play a prominent role in medical therapy. This compound and its derivatives are used in the treatment of rheumatism and gout, as antipyretics, keratolytics and analgesics. Because of their widespread use and ease of purchase, the annual consumption of salicylates indicates that they constitute some of the most extensively used medications in the United States. Used properly, salicylates are effective and rarely cause harmful or fatal reactions. However, in excessive dosage, the possibility of intoxication exists. The May 1961 Newsletter of the National Clearinghouse of Poison Control Centers recorded approximately 166,000 cases of salicylate intoxication.[1]

Absorption

Acetyl salicylic acid is absorbed from the stomach at a rate comparable to that of ethanol. It has been shown that in acid gastric fluid, salicylates return to an unionized salicylic acid form.[2] The unionized compound is then absorbed by a process of passive diffusion from the gastrointestinal tract.[13] The use of an alkalinizing agent, which raises the pH of the gastric juice, decreases the rate of absorption of salicylates. There is evidence that any factor which increases the rate of gastric emptying will increase the absorption rate of salicylates. An augmented absorption rate has been found to occur when the substance is administered with large volumes of fluid.[2] After salicylate is absorbed into the plasma, it moves into the tissues. However, since the rate of absorption into the plasma is much faster than its removal by the tissues, there is a disproportionately high plasma level of serum salicylate after ingestion.[3] In normal individuals, the peak plasma salicylate level occurs about one hour after oral ingestion.[4]

Excretion

The excretion of salicylate is primarily through the kidneys. After its absorption from the upper gastrointestinal tract, salicylate can be found in the urine within twenty minutes.[4] Studies done on the degradation,

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Presented as a Medical Grand Rounds at Mt. Sinai Hospital, Minneapolis, November 24, 1964.

Continued

conjugation and excretion of salicylate show that approximately 70 to 80% is excreted in the urine in the form of free salicylate and its metabolites. A portion of the salicylate is bound to serum albumin, while the rest diffuses throughout the body water. Detoxication is accomplished in part by conjugation with glycine and glucuronic acid, with excretion in the urine in this conjugated form.[4] Approximately 20% of salicylate is excreted unchanged, 50 to 55% as salicyluric acid, 1% as gentisic acid, and 15 to 40% as glucuronic acid conjugates.[5] The excretion of free salicylate is increased in an alkaline urine. When the pH of urine is 7.5 or greater, 80% of the salicylate is excreted in the free form.[4]

Toxicity

Most surveys have shown poor correlation between serum salicylate level and severity of toxicity. There is no single toxic dose for all individuals. In some persons, levels as low as 20 mg.% have resulted in fatal intoxication, whereas other individuals are asymptomatic at the same serum level.[4] Nausea, vomiting, erythema, deafness and tinnitus have been associated with serum levels of 20 to 30 mg.%. At levels of 30 to 40 mg.%, albuminuria, profuse sweating, vertigo and hyperventilation have been recorded. Stupor, confusion, dyspnea and pulmonary edema begin at levels from 40 to 50 mg.%. In general serum levels greater than 50 mg.% are invariably toxic.[7]

Clinical Severity

Done[8] attempted to categorize the severity of salicylate intoxication on clinical grounds without reference to salicylate levels, as follows: 1. *Asymptomatic* — Subjective but no objective manifestations. 2. *Mild* — Mild to moderate hyperpnea, sometimes lethargy. 3. *Moderate* — Severe hyperpnea, prominent neurologic disturbance (marked lethargy and/or excitability) but neither coma nor convulsions. 4. *Severe* — Severe hypernea, coma or semicoma with or without convulsions. He felt that the variable of time determined the relationship between salicylate level and the severity of intoxication. Experiments following the oral ingestion of aspirin showed that the decrease in serum salicylate level approximated that of a first-order reaction. Beyond three hours, the serum salicylate level was found to decline at a constant fractional rate which did not change over twenty-four hours.

With the knowledge that the serum salicylate level at a given time could be accurately determined, and that the disappearance of salicylate from the serum was a first-order reaction, the half life of the circulating salicylate could be calculated. Half-life values, which ranged from fifteen to twenty-nine hours with a mean of twenty hours, were obtained. This made possible the extrapolation of the salicylate level back to zero time (So). Done then compared the clinical findings with the calculated So values. The correlation between the salicylate level at So and the severity of toxicity was excellent.

1. Asymptomatic	So 36 — 69 mg.%
2. Mild	So 56 — 89 mg.%
3. Moderate	So 84 — 111 mg.%
4. Severe	So 130 — 142 mg.%
5. Fatal	So 160 — 183 mg.%

From this study, it was concluded that a fatal outcome was inevitable in patients with an So value greater than 160 mg.%, unless rapid decrease was accomplished.

With the average rate of elimination of salicylate determined and with the relationship between So and the severity of intoxication established, a nomogram (Figure 1) was derived, making it possible to determine the expected severity of intoxication from the measured serum salicylate level at a given time after ingestion. The nomogram is not applicable to persons who have ingested salicylate in more than one dose. It is also unreliable in persons who excrete salicylate either faster or slower than average. The nomogram begins at six hours because earlier than this, the measured salicylate level approximates the So level and can be used directly in predicting the severity of intoxication. The use of the nomogram is of value in determining when vigorous therapy is necessary.

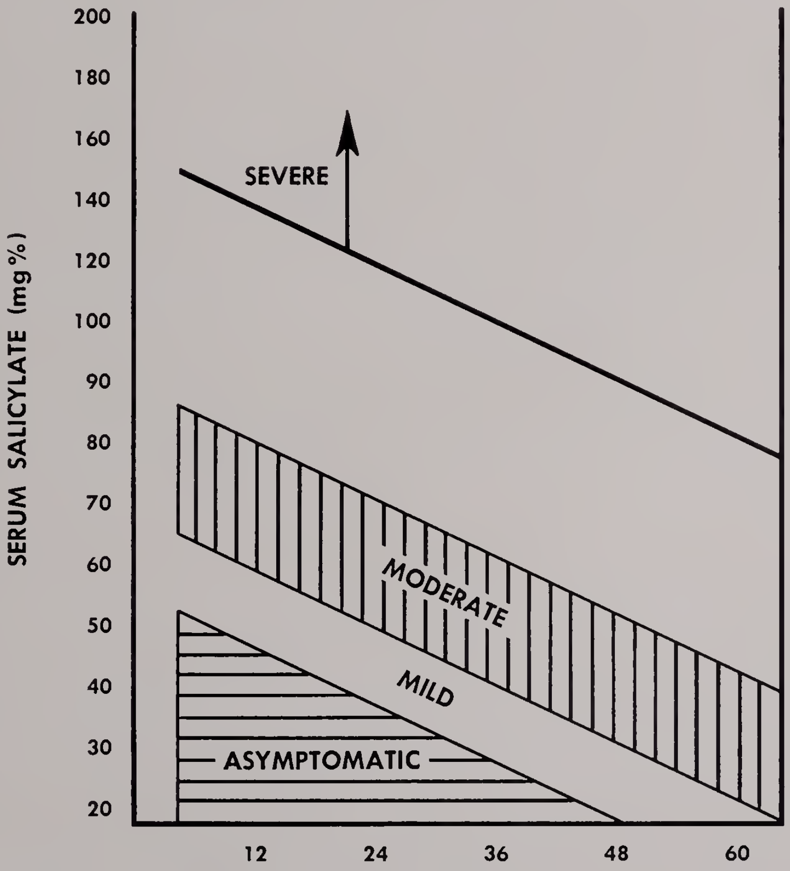

Fig. 1 — Nomogram of serum salicylate levels extrapolated from known level at any time after ingestion.*

Hyperventilation

Most clinicians regard hyperpnea as a valuable early sign of salicylate intoxication. Graham and Parker found that the hyperpneic action of salicylates was not seen if the serum level was below 21 mg.%. They felt that this toxic manifestation became evident at a serum level of 33 mg.% or higher.[9]

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*Reproduced from Done, A. K.: Pediatrics 26:800, 1957.

Continued

The mechanism producing hyperventilation secondary to salicylate intoxication has been investigated extensively. Initially it was thought that a transient lowering of blood pH initiated hyperpnea.[10] However, in experiments with animals, a transient lowering of the pH could not be demonstrated prior to the onset of hyperventilation. Stimulation of respiration was noted before the plasma CO_2 combining power began to fall. It was also observed that large doses of alkali failed to inhibit the stimulating action of salicylate on respiration.[9]

Other experiments indicated that neither the extirpation of the carotid bodies nor the administration of atropine abolished the stimulatory action of salicylates. However, when bilateral vagotomy was done, salicylates failed to produce hyperpnea. It was concluded that hyperventilation was due to the reflex stimulation of the respiratory center through the afferent fibers of the vagus nerve.[9]

A direct stimulating action of salicylates on the respiratory center was also demonstrated. This action was shown to be independent of the aortic and carotid chemoreceptors. When low concentrations of salicylates were applied directly to the region of the medulla by a needle in the cisterna magna, a rapid and dramatic increase in ventilation occurred.[10] It was also observed that the anterior hypothalamus was able to mediate the action of salicylates on respiratory stimulation.[11] A lesion in this region was capable of reducing or abolishing the stimulatory effect of salicylates.

Tenny and Miller have concluded that the respiratory response to salicylates is due to a direct central stimulating action and to the increased metabolic production of CO_2.[10]

Eichenholz et al. believe that the initial hyperventilation is due to the stimulatory effect of salicylates on the medullary respiratory center.[12] They concluded that the hyperpnea which persists in the metabolic acidosis phase of intoxication is brought about by respiratory center stimulation by an acid pH.

Metabolic Effects

A common observation in all cases of salicylate intoxication is a significant rise in oxygen consumption. A two-fold increase in O_2 consumption has been recorded in some cases.[10] The increased O_2 requirement has been found to be independent of central and peripheral nervous control. The use of epinephrine antagonists does not affect the metabolic response; decapitated animals show an increased metabolic response. It is thought that the site of the metabolic activity is in the skeletal muscles.[10] Salicylates apparently are able to stimulate cellular metabolism directly. The net result of this increased metabolic activity is cellular hypoxia, despite hyperpnea and increased cardiac output. The hyperpyrexia, seen in salicylate intoxication, is believed to be secondary to increased metabolic activity.[4]

Acid-Base Disturbance

The usual acid-base disturbance in salicylate intoxication is initially respiratory alkalosis followed by metabolic acidosis. The respiratory alkalosis is secondary to increased pulmonary loss of CO_2 due to hyperventilation with subsequent decrease in blood CO_2.[4] Associated with the alkalosis is the development of hypokalemia. Robin and co-workers[11] reported four cases of salicylate intoxication with respiratory alkalosis and hypokalemia, and EKG changes consistent with hypokalemia. With the administration of potassium the EKG returned to normal. Neuromuscular disturbances were also observed which disappeared when potassium was given. In their cases, Robin and co-workers failed to see the development of metabolic acidosis in patients receiving adequate potassium therapy.

Some believe that acidosis in salicylate intoxication is due to a ketosis, which occurs as a result of poisoning of the Krebs cycle. Alpha-Keto-glutaric dehydrogenase and succinic dehydrogenases are apparently inhibited, blocking the conversion of alpha-ketoglutarate to succinate and from succinate to fumarate. These blockades then allow keto acids to accumulate, resulting in acidosis which inhibits the renal excretion of salicylates.[4]

Eichenholz and co-workers report that the acidosis of salicylate intoxication is due to the progressive bicarbonate deficit associated with an increase of lactic and pyruvic acid.[12] Mechanical hyperventilation without salicylate intoxication is also capable of producing metabolic acidosis with a rise in serum lactic and pyruvic acid. Experiments on fully anesthetized dogs with complete muscular relaxation showed that during the course of hyperventilation, bicarbonate fell and lactic and pyruvic acid levels rose, unless 4% CO_2 was present in the inspired air. Dogs who received 4% CO_2 in the inspired air showed no drop in serum bicarbonate and no rise in the lactic and pyruvic acid levels, and did not develop metabolic acidosis. From their studies, Eichenholz and co-workers concluded that a significant correlation existed between the fall in serum bicarbonate and the rise in blood lactate and pyruvate levels. Thus, it appears that metabolic acidosis in salicylate intoxication is due mainly to the accumulation of pyruvic and lactic acids. The mechanism by which reduced PCO_2 is able to cause a rise in pyruvic and lactic acid levels is not known.

The acidosis of salicylate intoxication has also been attributed to renal failure with accumulation of sulfate and phosphates. However, this is considered to be an uncommon and late manifestation of salicylate intoxication.[14]

Other Manifestations

Nausea and vomiting have been commonly observed in salicylate intoxication. Both central nervous system stimulation and local gastric irritation have been thought to be factors. It has been shown that administration of salicylates intravenously causes nausea and vomiting without the presence of salicylates in the gastric fluid.[15] Other experiments have indicated that nausea and vomiting occur at lower plasma levels when salicylates are given orally, than when administered intravenously.[13]

Gastric

Gastrointestinal hemorrhaging has also been noted in patients with salicylate intoxication. Epithelial desquamation and focal necrosis of the gastric mucosa are believed to contribute to the bleeding.[16] Studies by Winkelman and Summerskill showed that salicylates have no effect on the secretion of HC by the stomach.[17] They also demonstrated that acid and pepsin secretion was not affected by the administration of intravenous salicylate.

Continued

Nervous System

Salicylates in large doses have produced a marked depression of the central nervous system after an initial stimulation. Manifestations such as disorientation, stupor, hyperactivity, convulsions, circulatory collapse, coma and respiratory failure have been recorded.[14]

Leukocytes

Leukocytosis ranging from 11,000 to 20,000 per cu. mm. have been reported. Leukocytosis was found in the more seriously intoxicated patients. However, there was no correlation between the serum salicylate level and leukocytosis.[14]

Kidneys

A nephrotoxic effect of salicylates has also been reported by Lawdor and co-workers. Acute renal failure, characterized by oliguria, hyperkalemia and azotemia followed by a diuretic phase, was observed in a patient with salicylate intoxication.[18] Scott and co-workers did experiments which showed that salicylates caused a shedding of cells from the renal tubular epithelium.[19] However, they concluded that there was no evidence of nephrotoxicity with chronic salicylate ingestion.

Hypoprothrombinemia has frequently been observed in patients with salicylate intoxication. Some consider the action of salicylate to be identical with that of dicumarol. Dicoumarin is also thought to break down into salicylic acid in the body. The prothrombinopenia in salicylate intoxication can be prevented by Vitamin K administration.[14]

Hypouricemia is another common occurrence in salicylate intoxication.[11] It is thought that salicylates inhibit the tubular reabsorption of urates. Another explanation may be that high salicylate levels inhibit the activity of the enzyme uricase used in the determination of uric acid. In cases where the diagnosis of salicylate intoxication is difficult to make, hypouricemia may be an aid in diagnosis.

Adrenals

The development of Cushing's syndrome has been reported secondary to the chronic use of salicylates. It has been noted that the salicylate radical is capable of depleting the ascorbic acid content of the adrenal gland. This response can be abolished by hypophysectomy and inhibited by adrenal cortical hormones.[21]

Lungs

Pulmonary edema secondary to salicylate intoxication has been recorded. In most cases, heart disease was also present. However, Granville and coworkers report a case in which pulmonary edema developed without evidence of congestive heart failure or heart disease.[22]

Pancreas

Hyperglycemia and glycosuria occur in salicylate intoxication, making the differentiation between diabetic acidosis and salicylate intoxication difficult.[23] Salicylates are capable of causing glycosuria and hyperglycemia in nondiabetic subjects. In diabetic patients, however, large doses of salicylates have been reported to decrease blood sugar; in the late 19th century, salicylates were used to treat diabetes. The explanation of this paradoxical action of salicylates is not known. Benedict's reagent, used in glucose measurements, is reduced by salicylates as well as glucose. A positive acetone test can also occur, since the ferric chloride diacetic test measures both salicylates and diacetic acid.

Brain

Brain damage secondary to salicylate intoxication has been reported.[24] Vascular and ganglion cell changes have been observed. Vascular changes included venous engorgement with perivascular hemorrhages extending beyond the perivascular space, and dilated and congested capillaries.

Treatment

As with other types of acute intoxication, the basic treatment is directed toward rapid removal and enhanced excretion of the causative agent. However, in salicylate intoxication, the acid-base disturbances must also be managed.

Gastric Lavage

Any unabsorbed salicylate should be removed from the gastrointestinal tract. Gastric lavage and the induction of emesis should be instituted immediately.

Shock

If shock is present, whole blood, albumin or plasma transfusions should be started. Albumin is able to combine with the salicylate, making it less toxic.[14]

Hemorrhage should be treated by blood transfusion and vitamin K.[14]

Eichenholz and co-workers consider barbiturates the drug of choice in combating hyperventilation.[12] Rappoport and Guest, however, believe that barbiturate and salicylate are synergistic in their toxic and depressant action on the central nervous system, and advise against their use.[25]

Fluids

Parenteral fluids containing sodium, potassium and glucose are essential. With large amounts of fluid, urinary excretion of salicylates is enhanced. The use of sodium bicarbonate has been advocated by some but large doses may produce reappearance of respiratory alkalosis.[14] In a study by Whitten, Kesaree and Goodwin, a 50% reduction in salicylate levels within two to five hours was reported, when sodium bicarbonate was given intravenously.[26]

The use of the carbonic anhydrase inhibitor, acetazolomide was shown by Feuerstein et al.[27] to be more effective in reducing blood salicylate levels than fluids alone.

Drugs

Israels and Davies have advocated the use of trihydroxymethylamino methane (THAM) in cases of salicylate intoxication.[23] THAM is an alkaline buffer amine capable of accepting hydrogen ions. This compound in-

Continued

creases urinary pH and causes diuresis of an alkaline urine, leading to excretion of weak acids like salicylates.

Additional therapy of salicylate intoxication includes exchange transfusions, peritoneal lavage and hemodialysis. James et al. carried out experiments comparing the above three methods.[29] With exchange transfusions, they found that at least two blood volumes had to be exchanged, making the procedure long and tedious. Sensitization reactions and hypocalcemia frequently occurred. Hemodialysis was found to be the most effective method of removing salicylates. Fifty per cent of the initial dose was removed within a four-hour period. Peritoneal lavage was the simplest method; however, the rate of salicylate removal was much slower with only 25% of the initial dose removed in four hours. The best dialysate solution was one which contained 5% albumin and 10% glucose. It was noted that during the period of treatment, the amount of salicylate excreted in urine often exceeded that removed by peritoneal dialysis or exchange transfusion. This, however, did not occur with hemodialysis.

Case Reports

Case 1

This patient, a 39-year-old white woman with past history of psychoneurotic behavior, child neglect and barbiturate intoxication on an accidental basis, was admitted to Mt. Sinai Hospital on September 28, 1964. Two days prior to admission, she had been seen in the Outpatient Department with the chief complaint of severe headache, insomnia and weakness. On September 28, she was admitted with the diagnosis of hysteria and hyperventilation syndrome. On September 29, she appeared somnolent and toxic without objective neurological signs. A spinal tap was done and cerebrospinal fluid found to be normal. Blood salicylate level was obtained seventeen hours after admission, during which time she had received no salicylates, and was reported to be 39 mg.%. Blood barbiturate level was 0. Skull X rays were negative. That evening her blood CO_2 content was 18 meq/l and a second blood salicylate lovel was 33 mg.%. Urine pH was 6, and arterial blood pH was 7.51. She was given 2000 ml. 5% glucose in water intravenously during the night, and all medications were stopped. The next morning she was more alert and without symptoms.

Subsequent pertinent laboratory data is summarized below:

September 29, 1964 — Salicylate, 39 mg.% and 33 mg.% (17 and 21 hours after admission respectively)
Hb, 14 gm.%, CO_2 18 meq/l
WBC, 11,500

September 30, 1964 — BUN 13 mg.%
Glucose 130 mg.%
Cl 104 meq/l
Na+ 140 meq/l
K+ 3.2 meq/l
Salicylate 12 mg.% (34 hours after admission)
Bb 0.3 mg.%
Thymol turbidity 2, Ceph. Floc. negative
BSP 1%
Alk p'tase. 9 K.A. units
Urine pH 5

The patient was asymptomatic during the remaining five days of hospitalization and was discharged on October 5, 1964. The half-life of salicylate excretion based on above values was approximately 11 hours, consistent with an extrapolated serum salicylate level of 125 mg.% on admission.

Case 2

This patient, a 43-year-old white woman, was admitted to Mt. Sinai Hospital on November 6, 1964, with a diagnosis of hyperventilation syndrome, beginning two days prior to admission. There was no history of cough, chest pain or upper respiratory symptoms. She had had chronic recurrent headaches and nervousness for many years and frequently used aspirin preparations to relieve her headaches.

Physical examination on admission revealed an apathetic woman with shallow, rapid respirations. Nose, throat and lungs were normal. The remainder of the physical and neurological examination was entirely negative.

Laboratory studies on admission included hemoglobin of 13.8 gm.%, leukocyte count of 7,200 and a negative chest X ray and electrocardiogram. On the day after admission, blood CO_2 content was reported to be 12 meq/l, serum potassium 2.8 meq/l, and fasting blood sugar 80 mg.%. A serum salicylate level, determined 30 hours after admission, was 24 mg.%, and venous blood pH 7.45.

The patient became asymptomatic and her respirations normal during the 12 days of hospitalization, without treatment. On the basis of the low blood CO_2 content, low serum potassium, elevated venous pH and serum salicylate of 24 mg.%, 30 hours after admission, associated with hyperventilation, a diagnosis of salicylate intoxication was made. Assuming a salicylate excretion half-time of 20 hours, the extrapolated serum salicylate level on admission would have been 70 mg.%.

Because this patient had received 100 mg. sparine intramuscularly 40 minutes prior to drawing blood for salicylate measurement, the possibility that sparine might be measured as salicylate was investigated. It was found that sparine does give a color reaction, but on a mg. for mg. basis the color is only 10 to 16% as intense as that produced by salicylate. Another patient, who had not received salicylates, was given 100 mg. sparine intramuscularly and measurable salicylate levels were not observed. In order to give a false serum salicylate level of 25 mg.%, the serum sparine level would have to be greater than 100 mg.%, a level unlikely even with the largest therapeutic dosage.

Both Cases 1 and 2 presented with a history of neurotic complaints and chronic headache. In neither patient was the diagnosis of salicylate intoxication considered on admission to the hospital. Patients presenting with this type of history associated with hyperventilation must be suspected of salicylate intoxication and the serum salicylate level measured. Frequently the patient taking large quantities of aspirin for headache minimizes the amount and does not give this information unless asked.

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15-29. can be obtained from Grand Rounds Editor at Mt. Sinai Hospital.

* * *

Few people are capable of expressing with equanimity opinions which differ from the prejudices of their social environment. Most people are even incapable of forming such opinions. — Albert Einstein

* * *

Greetings!

Don't tell your friends about your indigestion: "How are you!" is a greeting, not a question. — Arthur Guiterman

* * *

If it wasn't for the optimist the pessimist would never know how happy he isn't.

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Abstracts, Briefs and Commentaries

POSTOPERATIVE PANCREATITIS

The authors have reveiewed a series of 52 patients who developed pancreatitis following surgery at the New York Hospital-Cornell Medical Center during the years 1939-1960. Their purpose is to emphasize that this is not too rare a complication, as well as to study the clinical features and assess factors that contribute to fatality.

Forty of the patients had preceding intra-abdominal operations, seven had procedures on the urinary tract, and the remaining five had procedures unrelated to the peritoneal cavity. The most common sites of initial operation were the stomach, biliary tract and the pancreas itself.

Clinical observations of these patients suggested the need to consider pancreatitis in a postoperative patient with pain out of proportion to the procedure, fever, and ileus. Tachycardia and abdominal mass were also frequently noted.

Many patients were reoperated under the impression that some other acute abdominal problem was present. The serum amylase will be a most helpful test in the differential diagnosis.

There were twenty-seven patients who survived the episode of pancreatitis. Six patients developed pseudocysts. Twenty-five patients died of postoperative pancreatitis. In review of autopsy findings it was felt that additional surgery might have benefited six of them. Five of the patients had prominent contributory causes to their death (superior mesenteric artery thrombosis, E-Coli septicemia, pyelonephritis, metastatic carcinoma of the parathyroid, peritonitis from colon perforation and abdominal carcinomatosis). Eleven of the expiring patients had evidence of hepatic dysfunction and nine had evidence of renal disease.

The authors conclude that the mortality rate is increased with the hemorrhagic form of pancreatitis and also in the presence of renal or hepatic dysfunction.

They believe that improvement in mortality rates may result from earlier diagnosis with prompt attention to fluid and nutritional requirements, and correction of complications amendable to surgery.

Robert N. Hammerstrom, M.D.
Minneapolis, Minnesota

Frey, C. F., and Beal, J. M.: Pancreatitis as a Complication of Operation. Arch Surg 87:1053, 1963.

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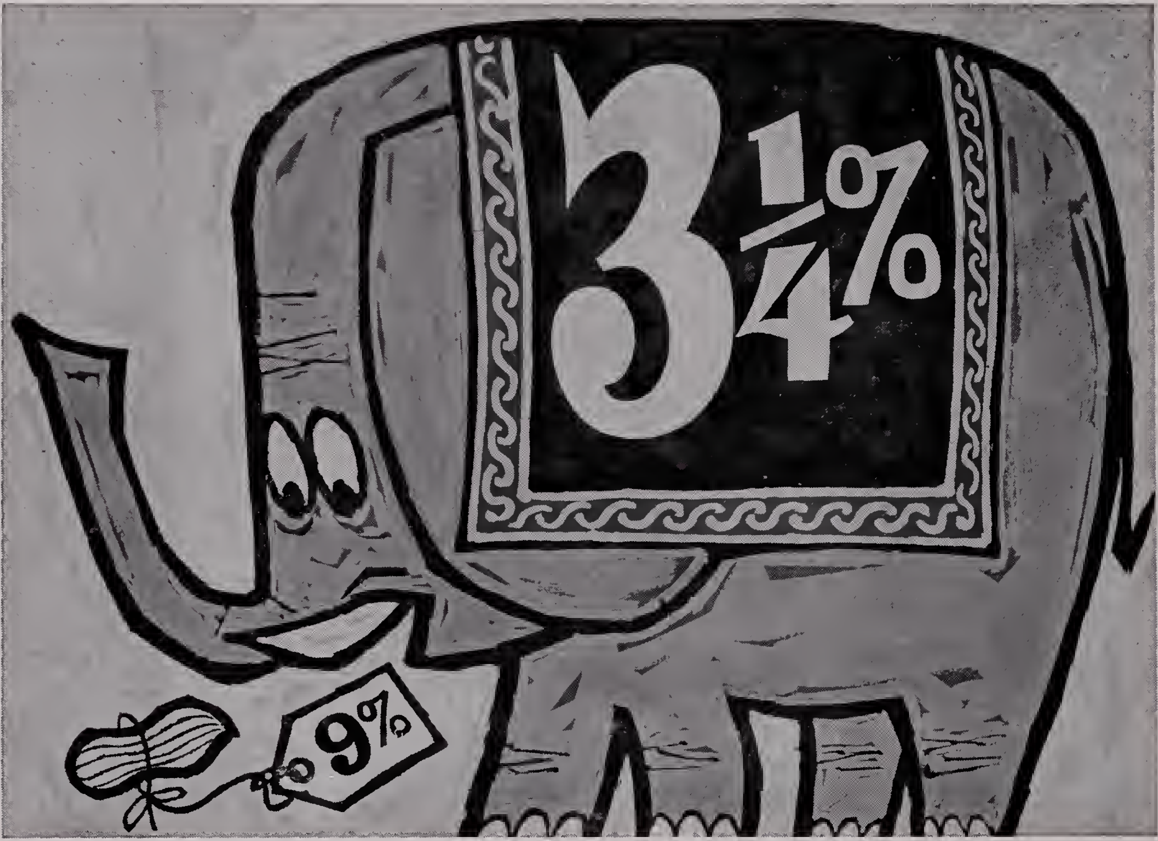

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PERIPHERAL ANGIOGRAPHY CLINICAL EVALUATION

The author believes that no one should be operated on for claudication unless he has been observed for at least a six-month period, as there are often spontaneous regressions. If there is, however, evidence of deterioration, then, of course, selective studies and necessary surgery should be carried out. In the University of Manchester, Department of Vascular Surgery, lumbar sympathectomy is used frequently and with good results, not for claudication but rather to prevent deterioration of the circulation to the foot and the skin. The author has never seen a case of "paradoxic gangrene" in approximately 1500 cases of lumbar sympathectomy and believes that this is not related per se to the procedure, but to vascular pathology in the opposite extremity.

The aortogram in *occlusive vascular disease* is of limited value and should be applied only in those cases in which there is doubt as to the diagnosis or where its use will either save the patient an operation or help define the need for surgical procedure. If there is evidence of an abdominal aneurysm over 7.5 cm. in diameter, rupture may occur and therefore this type should be resected. The author prefers the translumbar percutaneous approach for aortography but also uses the retrograde Seldinger technique.

In the femoral popliteal segment it is most important to combine the clinical examination, oscillometry, and judgment as to the need for angiography. At the time of operation the femoral popliteal segment should not only be explored, but injection of contrast below the block in the popliteal artery may be desirable to note the "run-off" of the distal arteries.

The author concludes by elucidating the two main principles in the surgical treatment of arterial disease: 1, Never run major risk to life and limb to cure minor symptoms, and 2, the feasibility of an operation is not necessarily an indication for it.

Jerome T. Grismer, M.D.
Minneapolis, Minnesota

Rose S.: Peripheral Angiography — Clinical Evaluation. Vascular Disease I:64, 1964.

CATHETERIZATION AND PERINEAL SHAVES

A familiar practice in almost every gynecologic service is the preoperative ritual of the perineal shave and bladder catheterization. Sweeney reports a study of 424 patients to determine whether these rites are necessary and harmless.

On admission to hospital each patient scheduled for curettage or completion of an incomplete abortion was labeled at random with a red or yellow card. The patients with a yellow card received a perineal shave whereas those with a red card did not.

The decision for catheterization was left to the operator. When this was performed the urine was collected and the amount recorded. It was less than 100 ml. in 70 percent of cases. Two methods of evaluation led to the conclusion that this amount does not interfere with the accuracy of pelvic examination under anesthesia.

Of the 424 patients 97 were admitted for completion of abortion and

Continued

327 for curettage. No patient with fever or other preoperative evidence of uterine or urinary tract infection was included.

The perineal shave was done by the nurses. The patient was anesthetized, the area was gently scrubbed with a skin cleanser containing hexachlorophene and was shaved with a sterile razor. Catheterization was done under anesthesia by the house officer; the introitus and urethral meatus were sprayed with a 10 percent povidone-iodine solution and a sterile glass catheter was passed.

There were no complications among 147 patients neither shaved nor catheterized, nor among 72 who were shaved but not catheterized. Four of the 67 patients who were catheterized but not shaved had postoperative urinary tract infections, and 7 of 138 who were both shaved and catheterized had similar complications. Postoperative catheter specimens showed pyuria in all 11 patients; *Aerobacter aerogenes* was cultured from all.

The results suggest the time-honored routine of catheterization before some gynecologic operations is unnecessary and potentially harmful. Also, for routine minor operations, such as curettage and completion of incomplete abortion, the perineal shave could well be eliminated. It was found to be unrelated to the subsequent absence or development of urinary, skin or pelvic infection.

Courtesy of World Wide Abstracts

Sweeney, W.: Obstet Gynec 21:3, 291.

ELIMINATION OF ROUTINE USE OF GASTRIC DECOMPRESSION FOLLOWING OPERATION FOR GASTRODUODENAL ULCER

During a 20-month period 130 patients were operated upon for ulcer disease, including vagotomy and either antrectomy or pyloroplasty. This group was then compared with a previous group of 130 patients in whom suction had been routinely employed. However, in 20 per cent of the group undergoing vagotomy operative findings dictated the use of suction; in the resection group, on the other hand, suction was employed in 11 per cent of the elective cases and in 70 per cent of the emergency cases. It is recommended that with any development of distention suction be instituted immediately.

The major conclusion of the study was to suggest that suction should not be employed routinely, but that definite indications, such as bleeding, emergency procedure, air swallowing, etc. should be considered as proper indications for its use.

There is no question of a trend toward less use of routine suction. However, this study is obviously highly selective when emergency cases and other problem cases are placed in the suction group, and the fact that these patients have fewer complications and slightly shorter hospital stays must be carefully assessed.

J. H. Strickler, M.D.
Minneapolis, Minnesota

Herrington, J. Lynwood, Jr., Edwards, William M., and Sawyers, John L.: Elimination of Routine Use of Gastric Decompression Following Operation for Gastroduodenal Ulcer. Ann Surg 159:807, 1964.

RENAL CARCINOMA

Recently it has been shown that many cases of renal carcinoma are not diagnosed. Many without hematuria have nonurologic symptoms, such as fever, loss of weight, and fatigue. Because of the presence of unusual symptoms, or the absence of symptoms, renal tumors are missed.

The authors of this report made a study of 4,563 autopsies in which renal carcinomas were found. Of these, carcinoma of the kidney was the primary cause of death in 42. Twelve were undiagnosed at the time of death— 29 percent. Forty-seven were incidental autopsy findings, termed "accidental," making a total of 59 (66 per cent) not diagnosed before death.

Renal carcinoma was found in two per cent of all autopsies in this series. Of these tumors termed accidental, 26 were in men and 21 in women.

In those in which renal carcinoma was the cause of death, 27 were men and 15 were women. The average age of patients with "accidental" findings was 74 years, while the average age of the group in which death was due to carcinoma was 67.

Renal carcinomas "accidentally" found varied in size from a pea to a large orange. All tumors in this study were confirmed as carcinoma by microscopic examination.

The findings in this report are based on the records from S:t Görans Hospital in Stockholm.

It would seem unusual that so many "accidental" diagnoses should occur. The writers in a review of the literature report spontaneous regression of the primary tumor and disappearance of metastases after removal of the renal carcinoma. In our own experience kidney tumors have usually been seen by us after the mass has become large and easily palpable. Some were too fixed for removal. One patient with a very large mass survived several years after nephrectomy. The authors reviewed current literature and quoted Dr. E. T. Bell.

Stanley R. Maxeiner, M.D.
Minneapolis, Minnesota

Bottiger, L. E., Hallberg, D., and Schreeb, T. V.: Renal Carcinoma As an Accidental Finding. Acta Chir Scand 127:158, 1964.

INTRAPERITONEAL DRAIN

From the Long Island Jewish Hospital in New York, Berliner et al. have carried out an interesting animal experiment to evaluate the use of drains from the site of an anastomosis.

As early as the turn of the century, Nikulicz doubted the value of intraperitoneal drainage and John L. Yates concluded that the peritoneal exudate from a drain is caused by its own foreign body reactions, and further stated that intraperitoneal drainage serves only the purpose of providing a path of least resistance under proper hydrostatic conditions.

Formerly it was more or less standard practice to introduce intraperitoneal drainage in colon surgery, but modern studies indicate that a drain may be harmful in that it prevents the sealing of an anastomotic leak by interposing itself between the suture line and the adjacent omentum.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Berliner, Stanley D., Burson, Leonard C., and Lear, Philip E.: Use and Abuse of Intraperitoneal Drains in Colon. Surgery 89:686, 1964.

HEMATOGENOUS METASTASES

A tumor suspension of VX-2 carcinoma of rabbits was inoculated into the thoracic aorta.

In the first experiment the spleen and perisplenic tissues were damaged by retrograde injection of nitrogen mustard into an isolated gastric branch of the splenic artery. Inoculations of tumor were made on varying days thereafter. It was found that splenic metastases were more frequent and more numerous to the extent of twenty-fold. Sixty-seven per cent of the test animals developed metastases to the damaged spleen and perisplenic tissues, compared to eight per cent in the controls. The greatest enhancement of this metastatic growth was seen between the second and fifth days after injury. This susceptibility continued to a slight degree for as long as one month after injury to the spleen.

The second experiment involved making abdominal wounds followed by an intra-aortic inoculation tumor. Some twenty times the expected inoculations or take-incidence occurred one week after injury to the abdominal wall.

The third experiment involved the effect of ischemic injury upon the formation of hematogenous metastases. This was a study of spleens damaged by ligation of the gastrosplenic vessels. Some 47 per cent of this group developed metastases to the gastric wall, a site that was assumed to have chronic ischemia by ligation of the gastrosplenic vessels. By comparison, only 5.2 per cent developed gastric metastases when these vessels were not ligated, but observed as part of another experiment where tumor cells had been injected.

In another study of the effect of wound closure with iodized catgut and wound metastases, no differences were found.

The effect of low molecular weight dextran upon the development of metastases was studied on the thesis that there might possibly be less adherence of tumor emboli through the small vessel walls. No aid was obtained.

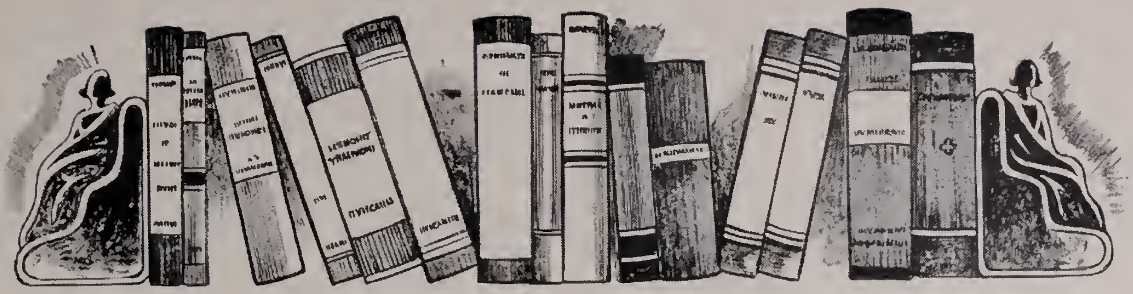
The authors feel that they have adequately demonstrated the increased susceptibility of damaged tissue to implantation of circulating tumor cells, and since some of the method of damage was employment of nitrogen mustard infusions, caution is suggested when regional profusion techniques are to be employed in the treatment of cancer.

J. H. Strickler, M.D.
Minneapolis, Minnesota

Alexander, J. Wesley, and Altemeier, W. A.: Susceptibility of Injured Tissues to Hematogenous Metastases. Ann Surg 159:933, 1964.

Writers seldom write things they think. They simply write the things they think other folks think they think. — Elbert Hubbard

Happiness sneaks in through a door you didn't know you left open.
— John Barrymore



Book Reviews

A human being is not, in any proper sense, a human being till he is educated.
— H. Mann

PEDIATRIC OPHTHALMOLOGY — **L. Byerly Holt, M.D., Lea & Febiger, 1964. 403 pages. $12.00.**

This book is intended to supply the pediatrician with a reference source for eye problems. Thirty-two contributing authors have provided 37 chapters on various aspects. Some of the material is excellent, but it seems a shame that the volume is so poorly organized, proofread, and edited. The sensitive reader may be annoyed by reading identical descriptions of the same disease twice in one chapter, or by being confronted with a chapter one page long. A second edition would be welcome, but until then the pediatric student may have to wade through the present one for lack of any better comprehensive book on the subject.

William S. McClanahan, M.D.
Minneapolis, Minnesota

X-RAY TECHNOLOGY — **Jacobi and Paris, Third Edition, C. V. Mosby Company.**

This edition is essentially the same as the second edition with the exception of updated illustrations and slight text revision.

Illustrations in general are too small and could be improved by better visualization of the central ray in two projections in those examinations which require such positioning. Multiple positions of a single part should not be included on the same page.

It is noted that some basic positioning variations are not given and that in most cases, Bucky and non-Bucky technique choices are not given. In regard to techniques, only variable tissue thickness techniques are mentioned with no listing of optimum or high KV techniques, except in a few isolated examples.

Photographic illustrations of anatomical models should be replaced with clear medical illustrations, as photographs of anatomical models do not reproduce well.

The absence of such technical factors as grid ratios employed leave a technical void.

There is a noticeable absence of detailed reference to the Mathematics of exposure, regarding the variables of MAS, time, KVP and distance.

This text is recommended for student technician training programs, but quick reference for working technicians is difficult, due to the inclusion of interesting but unnecessary information.

Eugene F. Inett, R.T.
Chief X-ray Technician
North Memorial Hospital

MEDICAL PHARMACOLOGY — **Andres Goth, C. V. Mosby Company, St. Louis, Missouri. 1964; 585 pages.**

While this book cannot serve as a reference text, it is a concise, well organized presentation of pharmacology as it relates to clinical practice.

The author has constructed the book so that one can abstract an outline from it, place any basic drug in that outline and have the site of action, mode of action and basic side effects immediately defined.

The book is divided into sections on central nervous system, cardiac, gastrointestinal, chemotherapeutic and metabolic drugs. Each of these sections is prefaced with some historical background and a discussion of the physiologic prospectus of the system that can be altered or enhanced with drugs. Following then, are a small profile of each basic drug and its mode of action on the physiologic mechanism.

The book is definitely constructed with the clinician in mind. It attempts to familiarize him with expected side reactions and actions of drugs he uses daily and gives him an idea of what to expect from so-called "new" drugs. With this knowledge, he will also be able to use drugs as tests of function of physiologic systems.

Jean R. Eckerly, M.D.
Minneapolis, Minnesota

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Special Article

Screening Preschool Children for Hearing Loss

EVELYN E. HARTMAN, M.D.*
Minneapolis, Minnesota

In a previous paper[1] preschool health-screening in Minneapolis' well-child clinics in 1961 was described. Prior to school entrance, preschool children attending well-child clinics of the Minneapolis Health Department receive a medical examination including a tuberculin test, followed at a later date by vision and hearing screening by nonmedical personnel, and laboratory tests for hemoglobin determination and urinalysis. Children who fail the vision and hearing screening are referred for further medical evaluation and treatment. A statement is requested from the hospital clinic or physician who sees the patient upon referral regarding treatment.

Prior to 1963 hearing screening was done with the Pure Tone Audiometer. It was not felt, however, that this was an ideal or completely reliable method of testing the hearing of young preschool children, although quite satisfactory for school-age children. It was hoped that a more objective method would become available.

Since January 1963, a Verbal Auditory method of screening the hearing of preschool children has been used in[1] the Minneapolis Health Department well-child clinics.[2] The method is one that had been devised for the Preschool Medical Survey of Vision and Hearing[3] sponsored by the Minnesota State Medical Association. The test is administered with the child seated before a picture board of 12 colored pictures, including such objects as a fire engine, a wrist watch, a bathtub, a snowman, a high chair and a sail boat. The child wears earphones connected with a magnetic tape audiometer. The male voice in the prerecorded and calibrated tape recording, starting at a volume of 51 decibels and decreasing by predetermined steps to 15 decibels, instructs the child to point to the various pictures. Each ear is tested separately. The monitor sits behind the child and hears the instructions

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*Director of Maternal and Child Health, Minneapolis Health Department.

Continued

through her own earphones; she can see whether or not the child points to the correct picture. The equipment permits two children to be tested at a time.

Prior to the screening the procedure is explained to the child in a simple manner and he is asked to identify the various objects. The names of pictures causing the most difficulty are "wrist watch" ("clock" to some children) and "bathtub" ("sink" to some children). The child is considered as failing the test if he does not respond to two of the three instructions at 15 decibels with each ear. If he fails the test and no other audio problems have been noted, a second screening is done at a later date, after which if he fails again he is referred to the physician.

This paper will compare results of hearing screening in Minneapolis Health Department well-child clinics in 1961 and 1962, when the Pure Tone Audiometer was used, with results obtained in 1963 when Verbal Auditory Screening was done with a magnetic tape audiometer.

Findings

Pure Tone Audiometer Screening Method

In 1961, 351 children (172 boys and 179 girls) completed their audiometric screening. Six other children were too immature or unco-operative to be tested. Another child who failed the tests had an upper respiratory infection when tested and was to be retested in school.

Of the 351 children, 335 passed the sweepcheck screening and another nine, who had failed the sweepcheck screening, passed the threshold testing. Seven children (2 per cent) failed the threshold test in one or both ears, or had hearing problems. A child was considered failing if he did not hear sounds at 20 decibels at two or more frequencies. Of the seven cases, four were previously known and included chronic otitis media, acute otitis media, frequent upper respiratory infections with hearing loss and frequent upper respiratory infections with earache. Of the seven children, two had tonsillectomy and four received other medical care.

In 1962,[4] hearing screening was completed for 377 children. Of these, 356 passed the sweepcheck screening and 10 the threshold test. Eleven children failed the test or had other ear problems; of these, four were previously known. Four other children could not be tested. Four children had tonsillectomy; four received other medical treatment. Of the latter, one child was admitted to a speech and hearing clinic and another needed special classroom seating. No treatment was necessary for two children.

Verbal Auditory Screening Method

In 1963, 248 boys and 228 girls "graduated" from Minneapolis Health Department well-child clinics prior to entering school in September and were referred for vision and hearing screening and laboratory tests at the Public Health Center.

Four hundred twenty-six children (219 boys and 207 girls) completed their hearing screening or had previously known ear problems; they are included in this report. Three other children were too unco-operative to be tested. Another eight failed the first test and did not return for rescreening.

TABLE I

Preschool Hearing Screening

	1961				1962		1963			
			Total		Total				Total	
Screened	M.	F.	No.	Per Cent	No.	Per Cent	M.	F.	No.	Per Cent
Passed Hearing Test (No Other Symptoms)	168	176	344	98.0	366	97.1	191	187	378	88.7
Failed Test or Had Other Ear Problems	4	3	7	2.0	11	2.9	28	20	48	11.3
TOTAL SCREENED	172	179	351	100	377	100	219	207	426	100

Of the 426 children, 337 passed the first hearing test and 41 who had failed the first test passed the second screening test. Forty-eight children (11.3 per cent) failed two tests or had previously known audio problems, nine of which were previously known. Of the 48 children who failed the test or had previously known problems, 38 followed through on their medical referral. For six of these (15.8 per cent of those completing the referral) no treatment was necessary. Diagnosed medical conditions included serous otitis media, impacted cerumen in ear canals, acute otitis media, congestion in Eustachian tubes, enlarged adenoids and tonsils. One child had severe hayfever with nasal discharge, watery eyes and head congestion. Three children had previously been known to have almost complete bilateral deafness and had been under special care. One of the three had developed normally, saying words at one year of age, but after an infection at 14 months of age her speech development had stopped.

Tonsillectomy was performed for nine children, and 23 children received medical treatment or were under continuing observation. Special education classes were necessary for the three children who had bilateral deafness, and special classroom seating was recommended for three children with hearing loss in one ear.

Discussion

Comparable groups of children between four and five years of age attending Minneapolis Health Department well-child clinics were screened for their hearing. Two per cent failed the hearing screening in 1961, 2.9 per cent in 1962, and 11.3 per cent in 1963. In 1961 and 1962, of the 18 children who failed the screening, eight had previously known problems. Two children (12.5 per cent of the 16 following through on their medical referral) needed no treatment. In 1963, nine had previously known audio problems. An additional 39 failed the screening tests. Six children who were referred for medical evaluation needed no treatment (15.8 per cent of the 38 children who followed through on the referral). In 1961 and 1962 there were thus six newly identified cases needing and receiving medical treatment, found through the hearing screening program with a yield of 0.8 per cent (among 728 screened), compared with 23 newly identified cases in 1963 (out of 426 screened) with a yield of 5.4 per cent. Although our figures are too small to make definite conclusions, we believe that 30 or 40 children needing treatment were missed by the method used for screening in 1961 and 1962.

Summary

Because of its objectivity and its higher yield of auditory deficiencies the verbal auditory screening method is recommended for screening the hearing of young preschool children by nonmedical personnel. In order to avoid unnecessary medical referrals it is recommended that a retest be done for a child failing the first screening.

TABLE 2
Follow-up of Those Completing Referral for Medical Evaluation

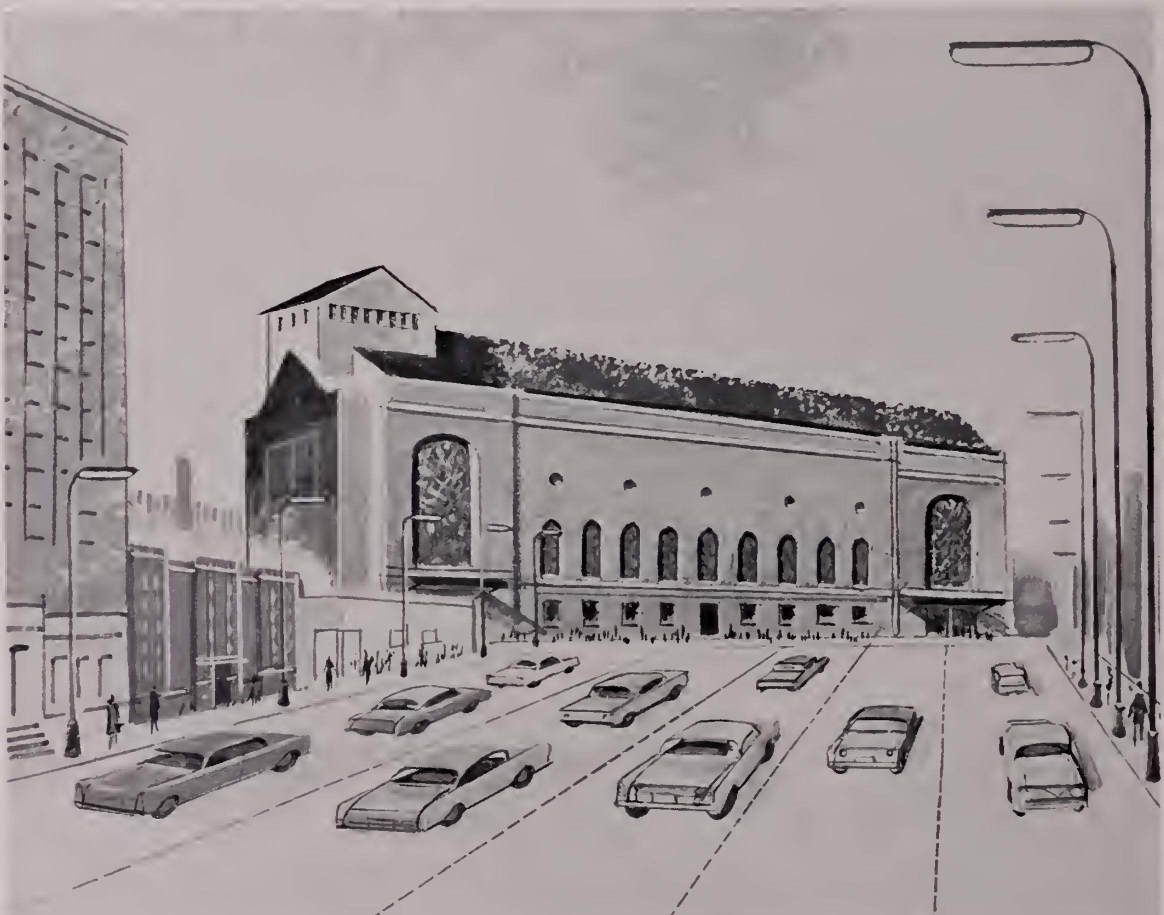
	1961			1962			1963		
	M.	F.	Total	M.	F.	Total	M.	F.	Total
No Treatment Indicated				1	1	2	5	1	6
Tonsillectomy	1	1	2	3	1	4	5	4	9
Medical Care	3	1	4	3	1	4	12	11	23
TOTAL COMPLETING REFERRAL	4	2	6	7	3	10	22	16	38

References

1. Hartman, E. E.: Preschool Health Screening in Well Child Clinics. J Sch Health 37:283, 1962.
2. Griffing, T. S., Simonton, K. M., Hedgecock, L. D.: Verbal Auditory Screening for Children. Minnesota Med 45:35, 1962.
3. Preschool Medical Survey of Vision and Hearing. Route 5, Stillwater, Minnesota. Executive Secretary Mrs. John R. Stoltze.
4. Previously unpublished data.

In Minneapolis . . .

WHERE MINNESOTA DOCTORS WILL BE IN '65



All roads lead to the auditorium!

112th Annual Meeting of the Minnesota State Medical Association

"The Doctor In Court," "The Need for the Medicine and Religion Dialogues," "Fractures In Children," "Relevance of the Spread of Cancer Cells to Chemotherapy" are among the topics of current medical interest scheduled for presentation at the 112th Annual Meeting of the Minnesota State Medical Association, May 17 and 18 in Minneapolis.

Scientific sessions and exhibits for a streamlined two-day meeting will be held in the Minneapolis Municipal Auditorium.

The House of Delegates will convene Sunday, May 16, at 2:00 P.M. at the Capp Towers Motor Hotel, 1313 Nicollet Avenue. The second session will convene Tuesday morning, May 18, at 9:00 A.M.

Four and one half hours Category I credit have been approved for members of the Minnesota Academy of General Practice for each of the two-day scientific sessions.

The opening scientific session, scheduled for Monday, May 17, at 9:00 A.M., will be devoted to a panel on the use of anticoagulants. Participating doctors at the opening session and their presentations are: "Indications and Contraindications" — John A. Spittell, Jr., Rochester, Moderator; "Laboratory Control of Anticoagulant Therapy" — C. A. Owen, Jr., Rochester; "Anticoagulant Therapy in Cardiac Disease" — M. W. Anderson, Rochester; "Anticoagulant Therapy in Cerebrovascular Disease" — R. G. Siekert, Rochester.

Because of the increased awareness of the need to create an interest and desire on the part of the physicians and the clergy to develop a common constructive approach in the care of the whole patient, the Committee on Scientific Assembly has arranged for a one-hour program on "Medicine and Religion" at 11:00 A.M. on Monday. Participants of both the panel and a medicine and religion round table luncheon will be Rev. Doctor Paul B. McCleave, Director, Department of Medicine and Religion, American Medical Association, and Dr. Orville S. Walters, Chairman of the Department of Student Health at the University of Illinois in Champaign.

"Fractures in Children" will be discussed by Doctor Albert B. Ferguson, Jr., Director, Children's Hospital, Orthopedic Department, University of Pillsbury, Pittsburgh, Pennsylvania, 2:00 P.M., at the opening afternoon session on Monday.

At 2:30 P.M., Doctor R. Gordon Bell, Executive Director, The Donwood Foundation, Ontario, Canada, will discuss "Alcoholism — Clinical Orientation to Addiction."

Doctor Leonard L. Lovshin, an internist from Cleveland, Ohio, will present the paper "How To Recognize Functional Disease" at the closing 4:00 session on Monday.

The scientific session for Tuesday, May 18, will constitute the Minnesota State Medical Association's observance of the 75th Anniversary of the University of Minnesota Medical School. Speakers for the Tuesday sessions will be members of the medical school faculty and alumni of world wide renown.

Doctor Raymond D. Pruitt, Professor and Chairman, Department of Medicine, Baylor University, Houston, Texas, will discuss "Cardiac Arrhythmias," at the opening Tuesday session at 9:00 A.M.

At 9:30 A.M. Doctor Claude R. Hitchcock, Minneapolis, is scheduled to present a paper on "Hyperbaric Oxygenation." A panel on "Relevance of the Spread of Cancer Cells to Chemotherapy" at 11:00 A.M. will include the following doctors: George E. Moore, Director, Roswell Park Memorial Institute, Buffalo, New York; B. J. Kennedy, J. B. Aust, and William Krivit, all of Minneapolis.

Tuesday afternoon scientific sessions will begin at 2:00 P.M. with a presentation by Doctor Jack V. Wallinga, Minneapolis. The title of Doctor Wallinga's presentation will be "Recognition of the Abnormal School Child."

The Honorable Warren E. Burger, Judge

Continued

of the United States Court of Appeals for the District of Columbia, Washington, D. C., will speak at 2:30 P.M. on "The Doctor In Court." At 3:30 P.M. Doctor W. B. Stromme, Minneapolis, will speak on "The Incompetent Cervix." A panel on the positive pap smear will climax the two-day program of scientific sessions. Panelists will include Doctors M. B. Dockerty, Rochester, Moderator; David C. Dahlin, Rochester; K. A. Prem, Minneapolis; and George J. D'Angio, also of Minneapolis.

Round table luncheons scheduled for Monday noon are: "What I Expect of the Physician in His Care of My Parishioners" and "What I Expect of the Clergyman in His Ministration to My Patients"; "Problem X-rays Related to Children's Skeletal Trauma"; "Drugs Affecting Human Behavior"; "Treatment of Burns" and "Treatment of Migraine."

The Tuesday schedule of Round Table luncheons includes the following subjects: "Current Electrocardiographic Concepts and Problems"; "Simultaneous Examination of Subject by Medical Experts before Testifying"; "Relevance of the Spread of Cancer Cells to Chemotherapy"; "Current Status of Medical Education"; "Socio-Economic Implications of Transplantations"; and "Counselling Parents of the Mentally Retarded."

American Medical Association President, Doctor Donovan F. Ward, will be the speaker Monday evening at the annual Minnesota Academy of General Practice banquet.

Following the Minnesota Academy of General Practice banquet, at 9:00 P.M. the Minnesota Chapter of the American College of Chest Physicians and the Minnesota State Medical Association will sponsor one of their Annual Fireside Conferences.

The Minnesota State Medical Association Annual Banquet scheduled for Tuesday, May 18, at 7:00 P.M. will climax the 112th Annual Meeting events.

The Third Duplicate Bridge Tournament to be held in conjunction with the Annual Meeting has been scheduled for Monday, May 17, at 9:00 P.M. The tournament is open to all players. Duplicate experience is not necessary. This will be a non-master point game. Trophies will be given for first and second place winners.

A number of the special events and social activities require advance registration. Physicians wishing to attend these events are requested to make arrangements in advance.

Many of the scientific and non-scientific committees have planned breakfast meetings in conjunction with our meeting. Kindly check the official annual meeting program for the date, time and place for your committee meeting.

Scientific Program
Minneapolis Auditorium

MONDAY, MAY 17, 1965

The program on Monday is acceptable for 4½ accredited hours by the American Academy of General Practice

A.M. Visit scientific and technical exhibits

9:00 **PANEL ON USE OF ANTICOAGULANTS**
Indications and Contraindications
John A. Spittell, Jr., Rochester
Moderator
Laboratory Control of Anticoagulant Therapy
C. A. Owen, Jr., Rochester
Anticoagulant Therapy in Cardiac Disease
M. W. Anderson, Rochester
Anticoagulant Therapy in Cerebrovascular Disease
R. G. Siekert, Rochester
Questions

10:15 Visit scientific and technical exhibits

11:00 **PANEL ON MEDICINE AND RELIGION**
Harold W. Hermann, Minneapolis
Moderator
The Need for the Medicine and Religion Dialogue
Reverend Paul B. McCleave, Chicago
The Dimensions of Medicine
Orville S. Walters, Urbana, Illinois
Questions

P.M.

12:15 **ROUND TABLE LUNCHEONS**

1:30 Visit scientific and technical exhibits

2:00 **FRACTURES IN CHILDREN**
Albert B. Ferguson, Jr., Pittsburgh, Pa.
Questions

Monday (continued)

2:30 ALCOHOLISM — CLINICAL ORIENTATION TO ADDICTION
R. Gordon Bell, Willowdale, Ontario
Questions

3:15 Visit scientific and technical exhibits

4:00 HOW TO RECOGNIZE FUNCTIONAL DISEASE
Leonard L. Lovshin, Cleveland, Ohio
Questions

9:00 FIRESIDE CONFERENCES

TUESDAY, MAY 18, 1965

The program on Tuesday is acceptable for 4½ accredited hours by the American Academy of General Practice.

A.M. Visit scientific and technical exhibits

Tribute to the University of Minnesota Medical School
J. M. Stickney, Rochester, President, Minnesota State Medical Association

9:00 CARDIAC ARRHYTHMIAS
Raymond D. Pruitt, Houston, Texas
Questions

9:30 HYPERBARIC OXYGENATION
Claude R. Hitchcock, Minneapolis
Questions

10:15 Visit scientific and technical exhibits

11:00 RELEVANCE OF THE SPREAD OF CANCER CELLS TO CHEMOTHERAPY
George E. Moore, Buffalo, New York
Moderator
B. J. Kennedy, Minneapolis
J. B. Aust, Minneapolis
William Krivit, Minneapolis
Questions

P.M.

12:15 ROUND TABLE LUNCHEONS

1:30 Visit scientific and technical exhibits

2:00 RECOGNITION OF THE ABNORMAL SCHOOL CHILD
Jack V. Wallinga, Minneapolis
Questions

2:30 THE DOCTOR IN COURT
The Honorable Warren E. Burger, Judge of the United States Court of Appeals for the District of Columbia, Washington, D.C.
Questions

3:15 Visit scientific and technical exhibits

3:30 THE INCOMPETENT CERVIX
W. B. Stromme, Minneapolis
Questions

4:00 PANEL ON THE POSITIVE PAP SMEAR
M. B. Dockerty, Rochester
Moderator
David C. Dahlin, Rochester
K. A. Prem, Minneapolis
G. J. D'Angio, Minneapolis
Questions

7:00 ANNUAL BANQUET
Presentations
Entertainment, Dancing and Late Evening Buffet

ROUND TABLE LUNCHEONS
CAPP TOWERS MOTOR HOTEL

MONDAY — 12:15 P.M.

Medicine and Religion
What I Expect of the Physician in His Care of My Parishioners
Rev. Paul B. McCleave, Chicago
What I Expect of the Clergyman in His Ministration to My Patients
Orville S. Walters, Urbana, Illinois

Problem X rays Related to Children's Skeletal Trauma
Albert B. Ferguson, Jr., Pittsburgh, Pa.

Drugs Affecting Human Behavior
Amedeo Marrazzi, Minneapolis
James Janecek, Jr., Minneapolis

Treatment of Burns
John F. Perry, St. Paul

Treatment of Migraine
Leonard L. Lovshin, Cleveland, Ohio

TUESDAY — 12:15 P.M.

Current Electrocardiographic Concepts and Problems
Raymond D. Pruitt, Houston, Texas

Simultaneous Examination of Subject by Medical Experts Before Testifying
The Honorable Warren E. Burger, Washington, D.C.

Relevance of the Spread of Cancer Cells to Chemotherapy
George E. Moore, Buffalo, N. Y.

Current Status of Medical Education
Robert B. Howard and
H. Mead Cavert, Minneapolis

Socio-Economic Implications of Transplantations
Richard L. Varco, Minneapolis

Counselling Parents of the Mentally Retarded
Reynold A. Jensen, Minneapolis

Sports Events

SUNDAY, MAY 16

GENERAL INFORMATION: Participants in sports events, their wives, and all who attend the Annual Meeting are invited to attend a sports events buffet at 5:00 p.m. at the Hazeltine National Golf Club, Chaska.

GOLF TOURNAMENT

PLACE: Hazeltine National Golf Club, Chaska

TEE-OFF TIME: 10:00 a.m. — 12:00 noon, Sunday
Prizes will be awarded to the low scorers. Green fees $7.50.

SKEET AND TRAP EVENTS

PLACE: Twin City-Hopkins Gun Club

TIME: 10:00 a.m. — 4:00 p.m., Sunday. Events will include skeet, trap and razzle dazzle. Prizes will be awarded for each.

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William Beaumont
(1785-1853)

New occasions teach new duties; Time makes ancient
good uncouth;
They must upward still, and onward, who would keep
abreast of Truth . . .
The Present Crisis
James Russell Lowell

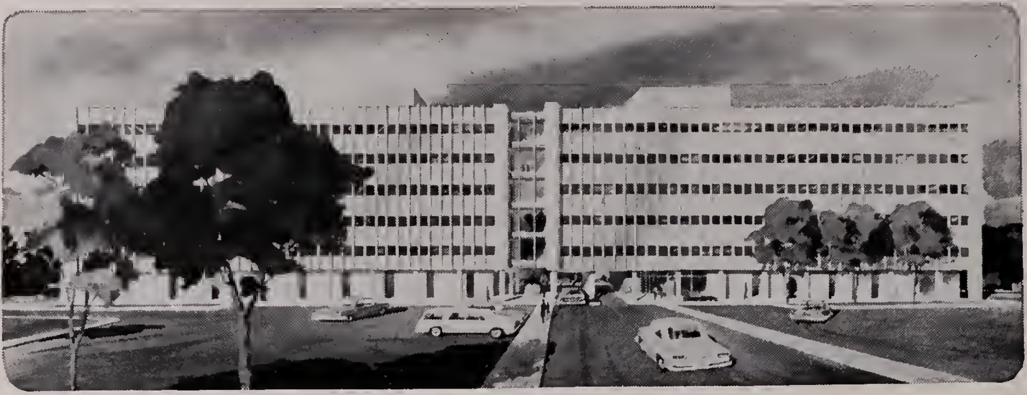
We know from history that great crises produce great men. In William Beaumont we have not only a great American surgeon, but also the first great American physiologist. He was born in the little colony of Lebanon, Connecticut, a farming community, which was just recovering from the Revolution. He grew up in this homespun environment, receiving a common-school education. In 1806, he left the family farm; ". . . setting out with a horse and cutter, a barrel of cider, and $100, he drove northward. . . Arriving at Champlain, New York, near the Canadian border, he was favorably impressed with the place, applied for and received the position of village schoolmaster, and taught there for three years. During these years, he decided to study medicine. He crossed Lake Champlain to St. Albans, Vermont, and became an apprentice and student of medicine under Dr. Benjamin Chandler. He remained with his preceptor for two years, preparing drugs, sweeping out the office, and assisting the doctor in his practice."[1]

A letter to his parents shows the knowledge and experience he was gaining there: "My situation affords me a very pleasant life, though it requires my utmost diligence and perseverance in the pursuit of a medical profession by which I hope to exhibit proficiency in an art which, in this enlightened age of reason and under the modern improvements of Chemistry and Physiology, bids fair to rise with healing on her wings."

Upon completing his apprenticeship, he was granted a license by the Third Medical Society of the State of Vermont, on June 2, 1812. When the War of 1812 began he joined the Army as Surgeon's mate in the Sixth Regiment Infantry. Beaumont's war diary yields some fascinating reading. "He describes 'the Surgeons wading in blood, cutting off arms, legs, and trepanning heads' after the Battle of Little York and notes, 'I cut and slashed for 48 hours without food or sleep.' He saw much fever in the army and criticizes one regimental surgeon who gave emetics and purges followed by tonics and lost 26 out of 400, while the next regiment with a diametrically opposite treatment lost no cases out of 600. He adds, 'No! depletion by blood-letting and antimonal sudorifices and diaphoretics, and an entire disuse of all tonic medicines, is the proper plan of cure.' Obviously, young Beaumont was a disciple of Benjamin Rush."[2]

In 1820 he was stationed at Fort Mackinac as post surgeon. The headquarters of the American Fur Company were there, which brought traders, rough voyageurs, and Indians to the village in large numbers. A peculiar accident in 1822, which will live on throughout medical history, took place in the crowded Fur Company store. A gun was accidentally discharged.

Continued



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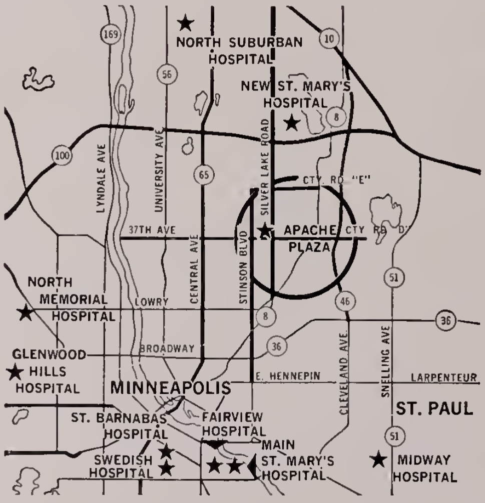
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The whole discharge, wadding and all, entered the body of Alexis St. Martin, a Canadian voyageur about 19 years old. He fell with a cavity in the left abdominothoracic region as large as a man's palm and an opening into the stomach cavity large enough to admit a forefinger. "Dr. Beaumont was immediately summoned and, after extracting some of the shot along with pieces of clothing, and after dressing the wound, left with the remark, 'The man cannot live 36 hours.' "[3] Beaumont's surgery was effective, and St. Martin, displaying remarkable vitality, began to mend. "Genuinely touched by the youth's misfortune, Beaumont took him into his family, nursed him, fed him, and clothed him—a real act of charity since Beaumont's salary at this time was only $40 a month with two to four rations daily, out of which he had to supply his own needs, those of Alexis and support his own family as well. Alexis recovered completely in two years, but the large fistula into his stomach remained."[4] He became the object of curiosity as the man with a lid on his stomach.

Before long Beaumont conceived the idea of using St. Martin as the subject of some physiological studies. Working at the Michigan frontier, with only the crudest experimental equipment available, he laid the foundation of our knowledge of the physiology of digestion.

(To be continued in May issue)

History of Medicine in Wright County*

Theodore F. Stark, was listed in Hasty as early as 1896 and may have stayed there until about 1898. Hasty is a small inland town, or group of houses, about five miles northwest of Monticello. He graduated from Jefferson Medical College, Philadelphia, in 1877 and was licensed in Minnesota December 31, 1883. He was in Big Lake, Sherburne County in 1896 for a short time.** From 1890 on he resided intermittently in Minneapolis where he is listed as late as 1905. No further information about him could be found.

Simon Peter Starritt, apparently practiced in Monticello for a while before moving to Anoka in 1880 or 1881. He was born in Hopewell, N. B. October 9, 1847 and came to Monticello with his parents in 1856 at the age of nine years. Between 1862 and 1865 he served in Hatch's battalion in the Indian campaign. Dr. Starritt graduated from the University of Minnesota in 1875 and from Hahnemann Medical College in 1878. About 1880, as mentioned, he moved to Anoka where he died two years later, January 3, 1883.†

John J. Catlin, M.D.
Buffalo, Minnesota
Robert Rosenthal, M.D.
St. Paul, Minnesota

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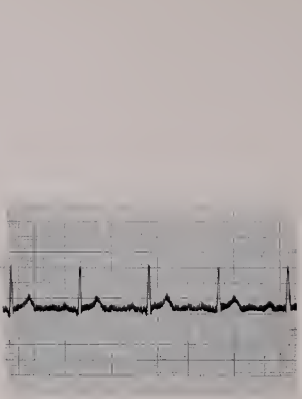
*See Minnesota Med 47:1565, 1964.

**"Medical History of Sherburne County prior to 1901" by Mrs. Josie M. Pfeifer and R. Rosenthal, M.D., Minnesota Medicine June 1961, p. 243.

†Upham and Dunlap, "Minnesota Biographies, 1655-1912."

Life's perhaps the only riddle that we shrink from giving up. — William Gilbert

AC can cause ECG problems



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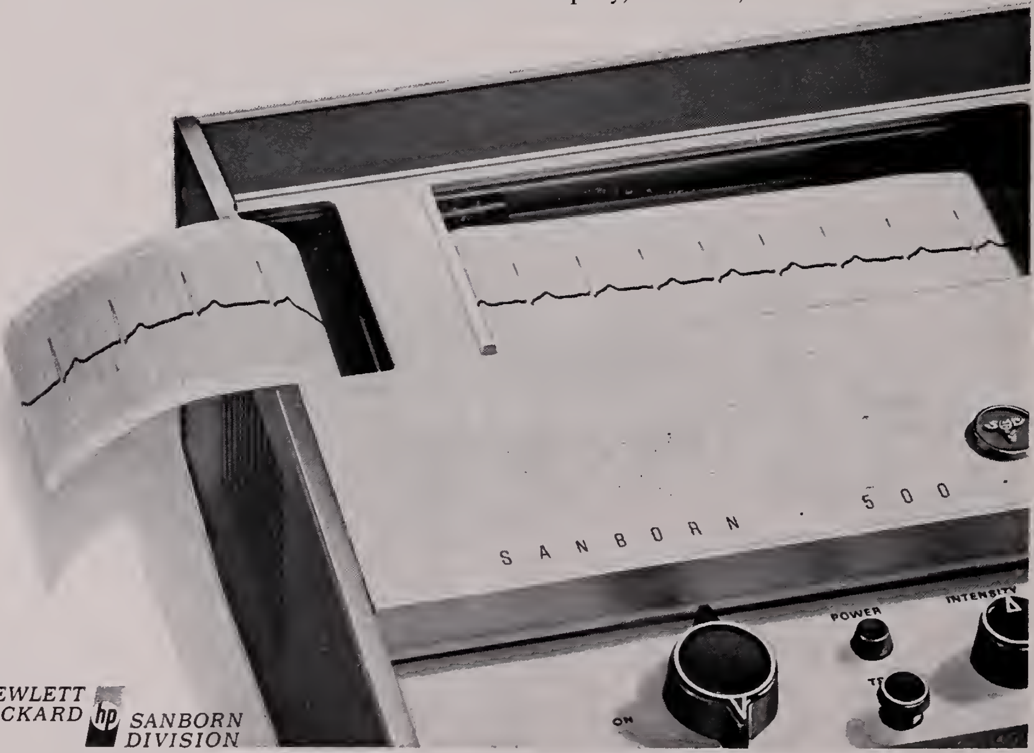

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Woman's Auxiliary

43rd Annual Meeting Plans Announced

All doctors' wives are cordially invited to attend the 43rd Annual Meeting of the Woman's Auxiliary to the Minnesota State Medical Association on May 17 and 18 in Minneapolis.

The Auxiliary meeting, held concurrently with the Association's 112th Annual Meeting, promises to be an especially interesting and exciting one. Members of the Hennepin County Medical Auxiliary, under the direction of their president, Mrs. T. B. Merner, will be hostesses for the event. Mrs. Richard C. Horns and Mrs. F. G. Gunlaugson, general chairmen, have announced plans for two busy days of activity, balancing business and pleasure with the opportunity to meet new and old auxiliary friends.

On Monday morning, May 17, auxiliary members may register from 9-10:00 A.M. at either the Curtis Hotel or the Minneapolis Auditorium. At 10:30 that morning the Executive Board Meeting will be held at the Curtis Hotel, followed at 1:00 P.M. by the Executive Board Luncheon, also at the Curtis. Monday afternoon at 3:00 P.M. the Auxiliary's Annual Tea will be held in the attractive Lutheran Brotherhood Building at 7th Street and 2nd Avenue, only two short blocks from Minneapolis' major stores. Registration facilities will be provided at the Lutheran Brotherhood Building for members unable to register earlier.

Monday evening at 9:00 auxiliary members will join with members of the Association for a Bridge Tournament at the Capp Towers Motor Hotel, headquarters for the Association's meeting. The Capp Towers, at 13th and Nicollet, is a short distance from the Auditorium, and is one of Minneapolis' most luxurious new hotels, featuring exquisite decor, sumptuous food, large indoor swimming facilities, and a unique glass-domed cocktail lounge which overlooks the lights of the city.

On Tuesday, May 18, the auxiliary's Annual Meeting will be held at 9:15 A.M. at the Minikahda Country Club on Excelsior Boulevard near Lake Calhoun. For members in need of transportation, rides will be furnished from downtown Minneapolis, beginning at 8:45 A.M. At 1:00 that afternoon, the Annual Luncheon will be held at the Minikahda Club. Mrs. William H. Evans, National Auxiliary President, will be honored guest and speaker.

That evening, the meeting will end with the Annual Banquet for doctors and their wives at the Capp Towers.

All doctors' wives, whether auxiliary members or not, are urged to attend this meeting, which promises to be stimulating, interesting, and fun-filled.

Remember — the Hennepin County Auxiliary wants you in Minneapolis on the 17th and 18th of May — so mark your calendar!

Mrs. Karl E. Johnson, President
Woman's Auxiliary to the
Minnesota State Medical Association

MONDAY, MAY 17

A.M.

9:00-10:00—Registration ....Curtis Hotel or Minneapolis Auditorium

10:30—Executive Board Meeting ......Curtis Hotel

P.M.

1:00—Executive Board Luncheon .....Curtis Hotel

3:00-4:30—Annual Tea .....Lutheran Brotherhood Building (registration for those not previously registered)

9:00—Bridge Tournament ....Capp Towers

TUESDAY, MAY 18

A.M.

9:15—Annual Meeting ...Minikahda Country Club
(Transportation from downtown Minneapolis at 8:45 A.M. will be provided)
Oral Reports
Election of nominating committee for the coming year
Election of officers

P.M.

12:00-1:00—Social Hour

1:00-3:00—Annual Luncheon ......Minikahda Club
Guest speaker—Mrs William H. Evans, National Auxiliary President

7:00—Annual Banquet ....Capp Towers

(This Program is Subject to Change. A More Detailed and Finalized Program will be sent to each Member before the Meeting.)

ANNOUNCING

112th annual meeting

FEATURING

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* Technical exhibits.

* Unusual scientific exhibits and demonstrations.

* Social and sports events.

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in minneapolis

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OFFICIAL PROGRAM & RESERVATION FORMS

To Be Mailed in April

Meetings and Announcements

If thou take delight in idle argumentation, thou mayest be qualified to combat with the sophists, but will never know how to live with men. — Socrates

APRIL

AMA second annual congress on environmental health problems, April 26-27, Drake Hotel, Chicago, Write: AMA-Chicago.

American Society for Study of Sterility, April 2-4, Jack Tar Hotel, San Francisco, California. Write: W. H. Robertson, M.D., 2700 Tenth Avenue South, Birmingham, Alabama.

Minnesota Obstetrical & Gynecological Society — 9:00 a.m., St. Luke's Hospital, Duluth.

St. Louis County Medical Society — Executive Comm. — April 8, 6:00 p.m., St. Luke's Hospital, Duluth, Regular Meeting — 8:00 p.m., St. Luke's Hospital, Duluth.

Minnesota Academy of Medicine — Regular meeting — April 8, 7:00 p.m., Town & Country Club, St. Paul.

American Academy of General Practice-Scientific Assembly — April 12-15, San Francisco.

Ramsey County Medical Society — Business & Program — April 26, 8:00 p.m., 15th Floor Lowry Medical Arts Building, St. Paul.

Thirteenth Annual Clinical Meeting of American College of Obstetricians and Gynecologists, April 5-8, Civic Auditorium, San Francisco. Write: The College, 79 West Monroe Street, Chicago.

American College of Surgeons ninth postgraduate course in trauma, April 28, 29, 30 and May 1. John B. Murphy Memorial Auditorium, 50 East Erie Street, Chicago. Write: John Fahey, M.D., 1791 Howard Street, Chicago.

National Association of Recreational Therapists, University of Wisconsin, Madison, April 4-9. Write: B. L. Smith, 500 Newton Rd., Iowa City.

Industrial Medical Association, American Hotel, Bal Harbour, Fla., April 5-8. Write Clark D Bridges, 55 E. Washington, Chicago 2.

MAY

Minnesota State Medical Association 112th Annual Meeting, Minneapolis Auditorium, May 17-18. Contact: Harold Brunn, 496 Lowry Medical Arts Building; St. Paul, Minnesota.

Woman's Auxiliary's breakfast, Capp Towers, Minneapolis, May 17, annual meeting, May 18, Capp Towers. Contact: Mrs. R. C. Horns, 4905 West Sunnyside Road, Minneapolis or Mrs. F. G. Gunlaugson, 121 West Elmwood Place, Minneapolis.

Hennepin County Psychiatric Society, May 3, 6:30 p.m., Leamington Hotel, Minneapolis.

Zumbro Valley Medical Society, May 5, Regular Meeting, 8:00 p.m., Plummer Hall, Rochester.

Minnesota Academy of Medicine, May 12, President's meeting, 7:00 p.m., Town & Country Club, St. Paul.

St. Louis County Medical Society, May 13, Executive Comm., 6:00 p.m., St. Mary's Hospital, Duluth. Regular Meeting, 8:00 p.m., St. Mary's Hospital, Duluth.

Minnesota Society of Internal Medicine, May 15, 9:00 a.m., Minneapolis.

Minnesota Society of Clinical Pathologists, May 17, 9:00 a.m., 4:00 p.m., Minneapolis.

Minnesota Chapter, American Academy of Pediatrics, Luncheon meeting, May 17, Minneapolis.

Minnesota Academy of General Practice, Annual May Banquet, May 17, Minneapolis.

Crippled Children Field Clinics:
May 4 — Detroit Lakes, National Guard Armory
May 11 — Mora
May 13 — Hibbing, National Guard Armory
May 20 — International Falls, Zion Lutheran Church
May 25 — Thief River Falls, Northwestern Hospital

ANNOUNCEMENTS

Part II examination will be conducted by the American Board of OB-GYN at Edgewater Beach Hotel in Chicago, April 26-May 1. Applications will be accepted in the office of the secretary during April and May. Contact: Clyde Randall, 100 Meadow Road, Buffalo, N. Y.

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Medical Economics

How Is Your Estate Planned?

Although a great deal has been written on the subject of estate planning, it is one that is often neglected. Proper estate planning often achieves thousands of dollars of estate-tax savings.

The marital deduction is the first step in a workable estate plan. Several years ago, provisions were established making it possible to reduce extra estate taxes substantially through the proper qualification of assets. These provisions grant a deduction from the gross estate equal to the value of property passing to the decedent's spouse outright, with full power of appointment, up to a limit of 50 per cent of the value of the estate.

By taking advantage of this deduction, one can add considerably to the share of a large estate that will actually become available to the beneficiary, and can effect substantial savings even on small estates.

For example, if Doctor Smith has assets valued at $120,000, use of the marital deduction could save $9,340 for his wife in the event of his death:

	Marital Deduction Not Used	Marital Deduction Used
Gross Estate	$120,000	$120,000
Specific Exemption	60,000	60,000
Net Estate	$ 60,000	$ 60,000
Marital Deduction (50 per cent of gross estate)	———	60,000
Subject to Tax	$ 60,000	None
Federal Estate Tax	9,340	None

Beware of the tax trap on large estates. Many men leave their entire estates to their wives, and if the gross value is in excess of $120,000 they incur tax losses. Remember that the marital deduction is limited to 50 per cent of the value of the estate. If you leave your wife a greater share, the property in excess of 50 per cent will be taxed in your estate, and will be taxed a second time in her estate if it has not been exhausted during her lifetime.

A way of avoiding this trap is to leave one's wife one-half the estate outright, to qualify for the maximum marital deduction, and then place the other half in a trust so designed as to give her all the benefits of the income and principal, but to avoid incurring taxes in her estate. Under such a trust, she can receive all income during her lifetime and can be paid sums from the principal for purposes stipulated in the trust agreement.

The remainder of the trust, upon her death, will pass untaxed to the beneficiaries originally named in her husband's will (usually the children). On a $200,000 estate, the tax pictures would be as follows:

	100% to Wife	50% to Wife 50% to Trust
Gross Estate	$200,000	$200,000
Specific Exemption	60,000	60,000
Net Estate	$140,000	$140,000
Marital Deduction	100,000	100,000
Doctor's Taxable Estate	$ 40,000	$ 40,000
Federal Estate Tax	$ 4,800	$ 4,800
Wife's gross estate, provided that she has lived on the income and has retained the entire principal.	$195,200	$100,000
Specific Exemption	60,000	60,000
Wife's Taxable Estate	$135,200	$ 40,000
Estate Tax	$ 31,000	$ 4,800
Tax Savings through Use of Trust		$ 26,200

Obviously, proper planning of your estate can thus mean many additional thousands of dollars for your family. You can see that technical errors could be quite costly. Thus, it is advisable for you to consult your attorney for help in setting up your program.

Most of us don't mind doing what we ought to do when it doesn't interfere with our doing what we want to do. — Cincinnati Inquirer

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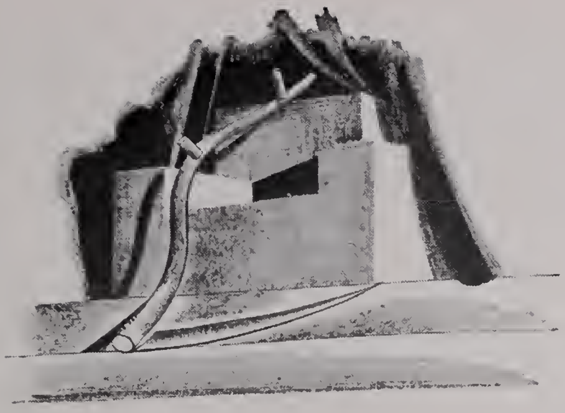

In Memoriam

A good man, when dying, once said, "Formerly death appeared to me like a wide river, but now it has dwindled to a little rill; and my comforts, which were as the rill, have become the broad and deep river."

We call it death to leave this world but were we once out of it and instated into the happiness of the next, we should think it were dying indeed to come back to it again.
— Sherlock

FRED W. WITTICH

Dr. Fred W. Wittich, 80, St. Louis Park physician, died February 4th. He was born in Carlysle, Pa., and was a graduate of Johns Hopkins University School of Medicine.

Dr. Wittich was the founder and first president of the International Association of Allergology and a former secretary-treasurer of the American College of Allergists. He was a fellow of the American College of Allergists, American Academy of Allergy, editor of the Review of Allergy and Applied Immunology, former faculty member of the University of Minnesota extension division and associated with the Glen Lake Sanatorium and Hennepin County General Hospital. He was a member of the Hennepin County Medical Society and American Medical Association and a life and 50 Club member of the Minnesota State Medical Association.

He is survived by his wife and two sons.

ALBERT E. OLSON

Dr. A. E. Olson, 69, prominent Duluth surgeon and a former University of Minnesota regent, died February 17th, unexpectedly in his home. He was born at Duluth and received his medical degree from the University of Illinois.

Dr. Olson served on the staffs of both St. Luke's and St. Mary's hospitals, was a life member of the American College of Surgeons, and a member of the St. Louis Medical Society, Minnesota State Medical Association and the American Medical Association.

He is survived by his wife and two sons.

MERCHISLAW M. SARNECKI

Dr. M. M. Saarnecki, 56, St. Paul surgeon, died February 10th. He was born at Cleveland, Ohio, and received his degree in medicine at Northwestern University Medical School.

He was on the staff at Ancker, Bethesda and St. John's hospitals, and was a member of the Ramsey County Medical Society, Minnesota State Medical Association and the American Medical Association.

He is survived by his wife and children.

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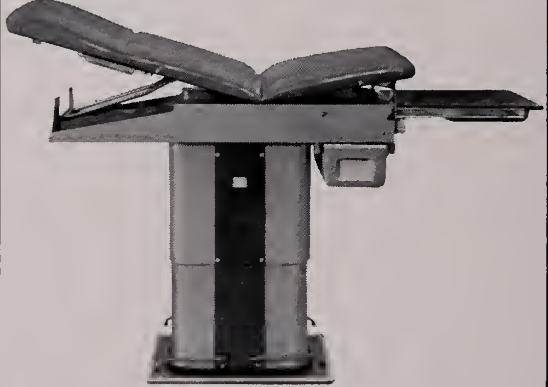

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Physician's Diary

> *Thou mayest be sure that he that will in private tell thee of thy faults, is thy friend, for he adventures thy dislike, and doth hazard thy hatred; there are few men that can endure it, every man for the most part delighting in self-praise, which is one of the most universal follies that bewitcheth mankind.*
>
> *— Sir Walter Raleigh*

Dr. W. A. Brand, 89-year-old Redwood Falls practicing physician, was named "outstanding senior citizen" of Redwood county by the board of commissioners in January. **Dr. P. L. Halenbeck** of St. Cloud was named Stearns county's "outstanding senior citizen" by the senior citizens council, and **Dr. F. E. Ellison** of Howard Lake was named Wright county's "outstanding senior citizen." These gentlemen will compete against entries from all counties in the state to name the State of Minnesota's "outstanding senior citizen."

* * *

Drs. Kurt Pollak, Henry L. Williams of Minneapolis and **Dr. Clifford F. Lake** of Rochester will be part of the instructional staff for the introductory course in "Expanded Surgery of the Nasal Septum" to be presented at the Methodist Hospital Graduate Medical Center, Indianapolis, April 21-24.

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Dr. A. Sigrid Halversen Gilbertsen of the Nicollet Clinic, Minneapolis, and **Dr. Arnold W. Fenske** of the Winona Clinic, Winona, addressed the American Association of University Women, Winona Branch, at their annual meeting in January. **Dr. Gilbertsen** spoke on "The Role of Heredity in Certain Blood Disorders," and **Dr. Fenske** spoke on "Pills and Progress."

* * *

Dr. Robert E. Peters of St. Paul was elected recently to the newly-created office of chairman of the board of directors of the Minnesota Heart Association.

Dr. D. L. Johnson of Little Falls was elected president of the St. Gabriel's hospital staff. Other officers elected were: **Dr. G. M. A. Fortier**, vice president, and **Dr. R. J. Stein** of Pierz, secretary-treasurer.

* * *

Dr. Ian Gregory, associate professor at the University of Minnesota, will become professor and chairman of the Department of Psychiatry in the Ohio State University College of Medicine, April 1st.

* * *

NEW LOCATIONS: **Dr. Richard Castillo** of Berkeley, California, has opened up a medical practice in Plainview . . . **Dr. Donald A. Bolt** of Tacoma, Washington, has opened up an office in the PBC Medical-Dental building, in Brooklyn Center . . . **Dr. Carl A. Schwartz**, formerly of Austin, now is associated with **Drs. W. S. Chalgren** and **J. B. Lund** in Mankato . . . The East Range Clinics at Virginia has announced the addition of **Dr. Wayne Johnston** to the professional staff . . . **Dr. Robert Pierce** of Mountain Lake has joined **Dr. George R. McNear, Jr.**, at the Heron Lake Clinic . . . **Dr. Clinton C. Rhodes** has joined the staff of the Itasca Clinic in Park Rapids. **Dr. Rhodes** has been interning at Ancker hospital in St. Paul . . . **Dr. R. E. Olson** has joined the partnership of the Valley Medical Clinic with **Drs. Gerald E. Nelson** and **Dr. G. T. Schimelpfenig.**

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Usual dosage: Adults – 250 mg. every six hours in respiratory infections; 500 mg. every six hours in urinary and gastrointestinal infections (higher doses may be needed in severe infections). Children – (under 13 years, whose weight will not result in a dosage higher than that recommended for adults) 100 mg./Kg./day in divided doses every six or eight hours for moderately severe infections; 200 mg./Kg./day in divided doses every six hours for severe infections.

Contraindications: (1) Hypersensitivity to penicillin. (2) Infections by penicillinase-producing staphylococci and other penicillinase-producing organisms.

Side Effects: Mild effects, such as skin rashes, diarrhea, nausea and vomiting have occasionally appeared.

Precautions: As with other antibiotics, precautions should be taken against gastrointestinal superinfection. To date, safety for use in pregnancy has not been established.

Supplied: No. 606 – Each capsule contains 250 mg. of ampicillin. Bottles of 16 and 100.

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WANTED: Internist to join well-established five-man group in town of 10,000 located in progressive area having good living conditions. Call or write: Alex Shadid, M.D., CA 5-2511, Elk City, Oklahoma.

TWO G. P.'s NEEDED — Northern Minnesota county seat; new hospital; office space available; two other physicians in town; anesthetist on hospital staff; good schools; all churches; excellent hunting and fishing; housing available; full details upon request. Contact: Administrator, Roseau Area Hospital, Roseau, Minnesota.

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If a man does not keep pace with his companions, perhaps it is because he hears a different drummer. Let him step to the music which he hears, however measured or far away. — Henry David Thoreau

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Triacetyloleandomycin, a constituent of Signemycin, administered to adults in daily oral doses of 1.0 Gm. (3 Gm. Signemycin) for periods of more than ten days may produce hepatic dysfunction and jaundice. In the rare patient who requires this high dosage level of Signemycin initially, liver function should be carefully followed and dosage should be reduced, as promptly as possible, to the usual recommended range of 1.0 to 2.0 Gm. per day. Therefore, Signemycin is recommended primarily for the treatment of acute or severe infections, with treatment restricted to a ten-day period. If clinical judgment dictates continuation of therapy beyond ten days, serial monitoring of the liver profile should be carried out, including BSP, transaminase, and cephalin flocculation tests. Changes observed in liver function were reversible following discontinuation of the drug.

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Note:

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Condition	No. of Patients	No. Responded To Signemycin
Ear, nose and throat infections	507	465
Respiratory infections	1,028	954
Gastrointestinal infections	425	387
Genitourinary infections	748	684
Skin and soft-tissue infections	1,088	1,036
Bone and joint infections	71	64
Deep-seated or generalized infections	257	251
Obstetrical & gynecological infections	341	320
Miscellaneous conditions	592	570
Totals	5,057	4,731 (93.5%)

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vhen a change in environment overwhelms him with anxiety

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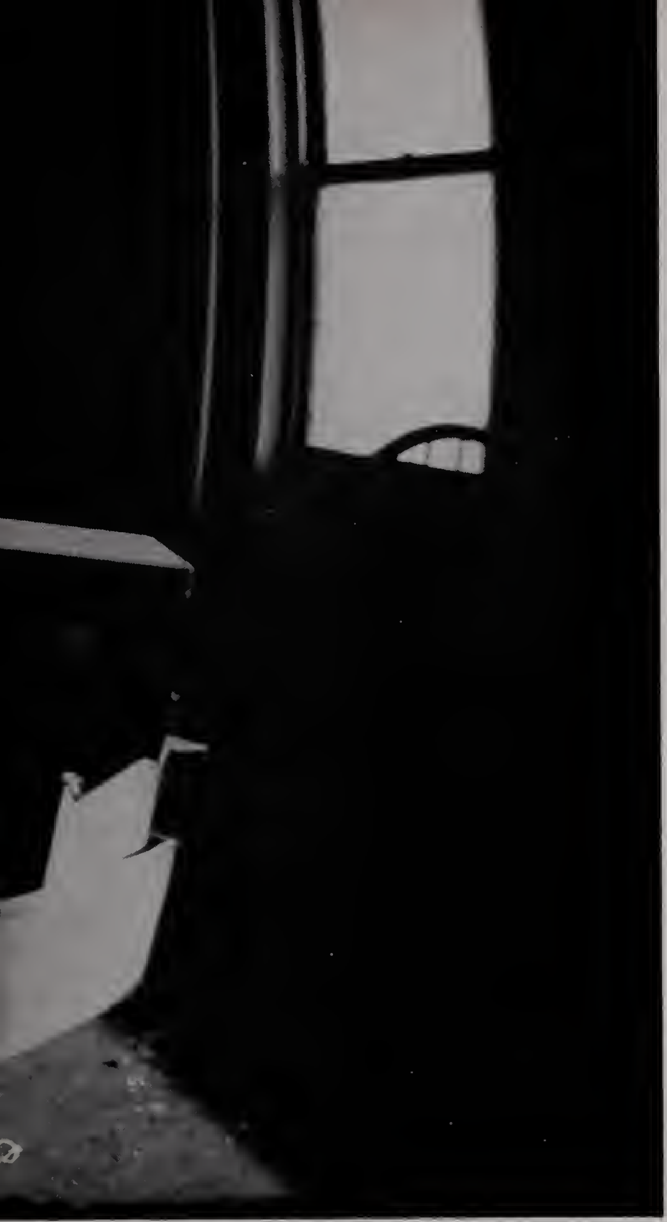

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1. Goodgold, J., Use of Nicotinic Acid-Glycine Mixture in Treatment of Peripheral Vascular Disease, Clinical Medicine 7:12 (1960).
2. Gustafson, Jr. et al. Use of Glycine in the Treatment of Peripheral Vascular Disease, Surgery 25:539 (1949).

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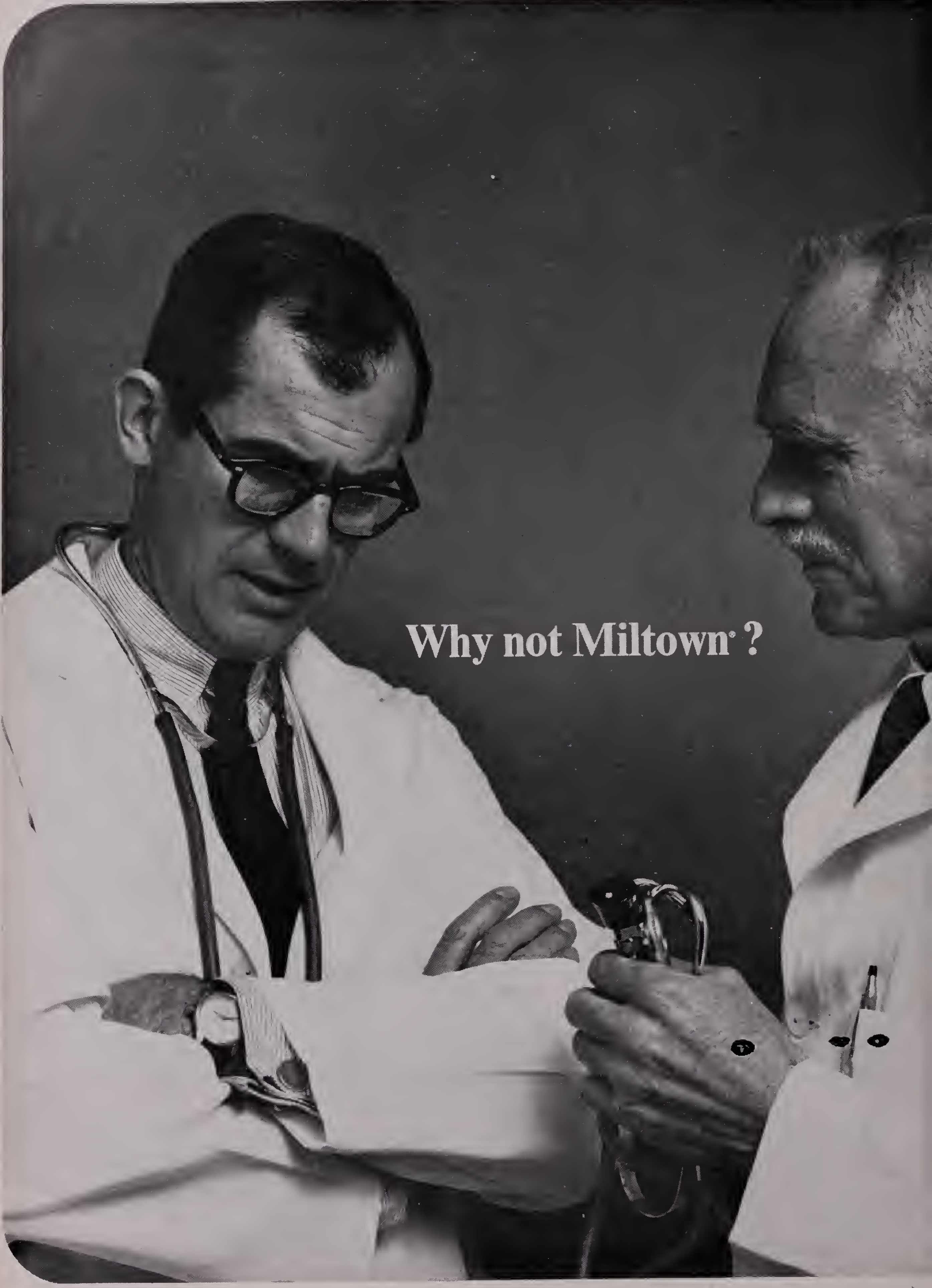
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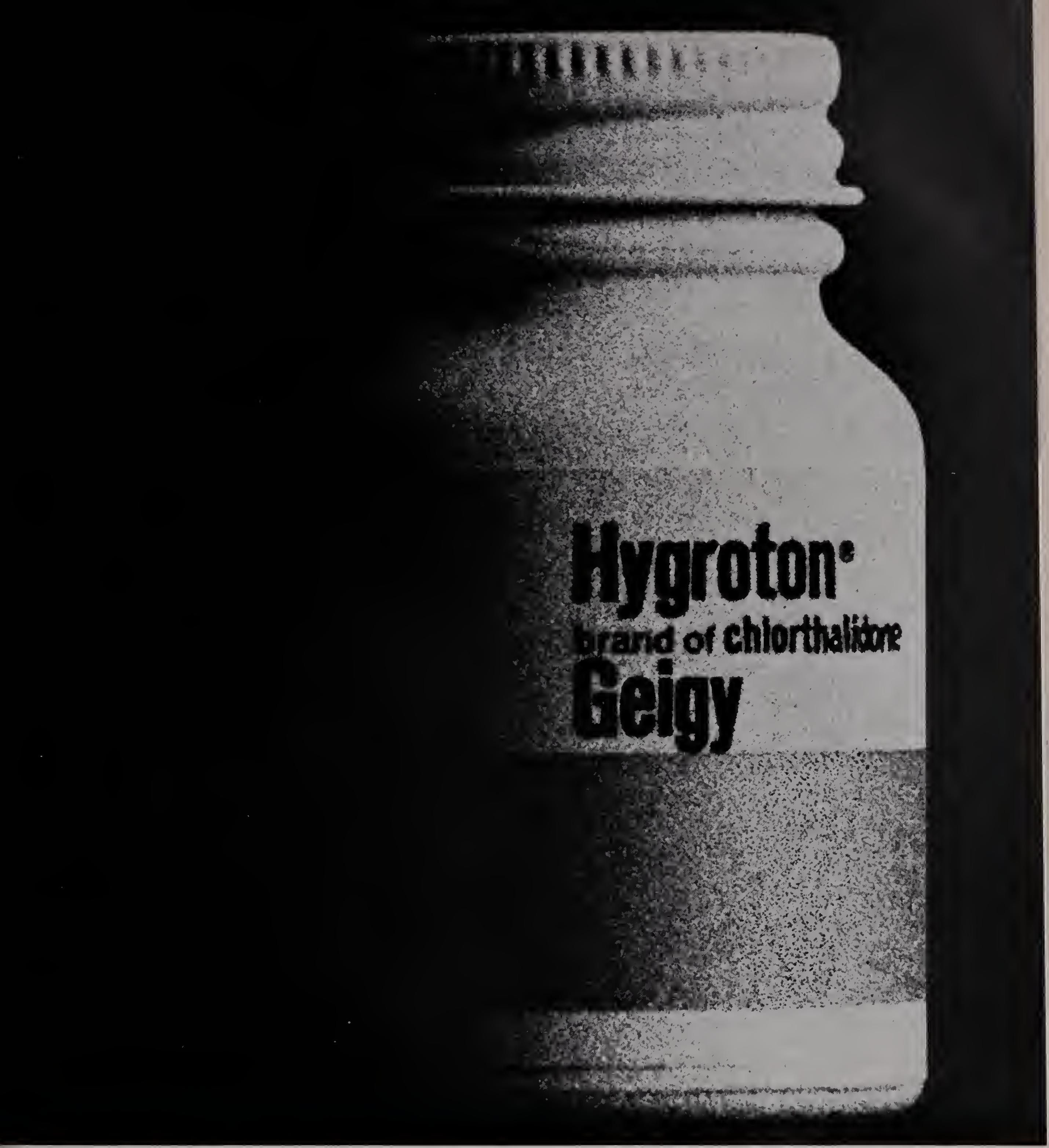

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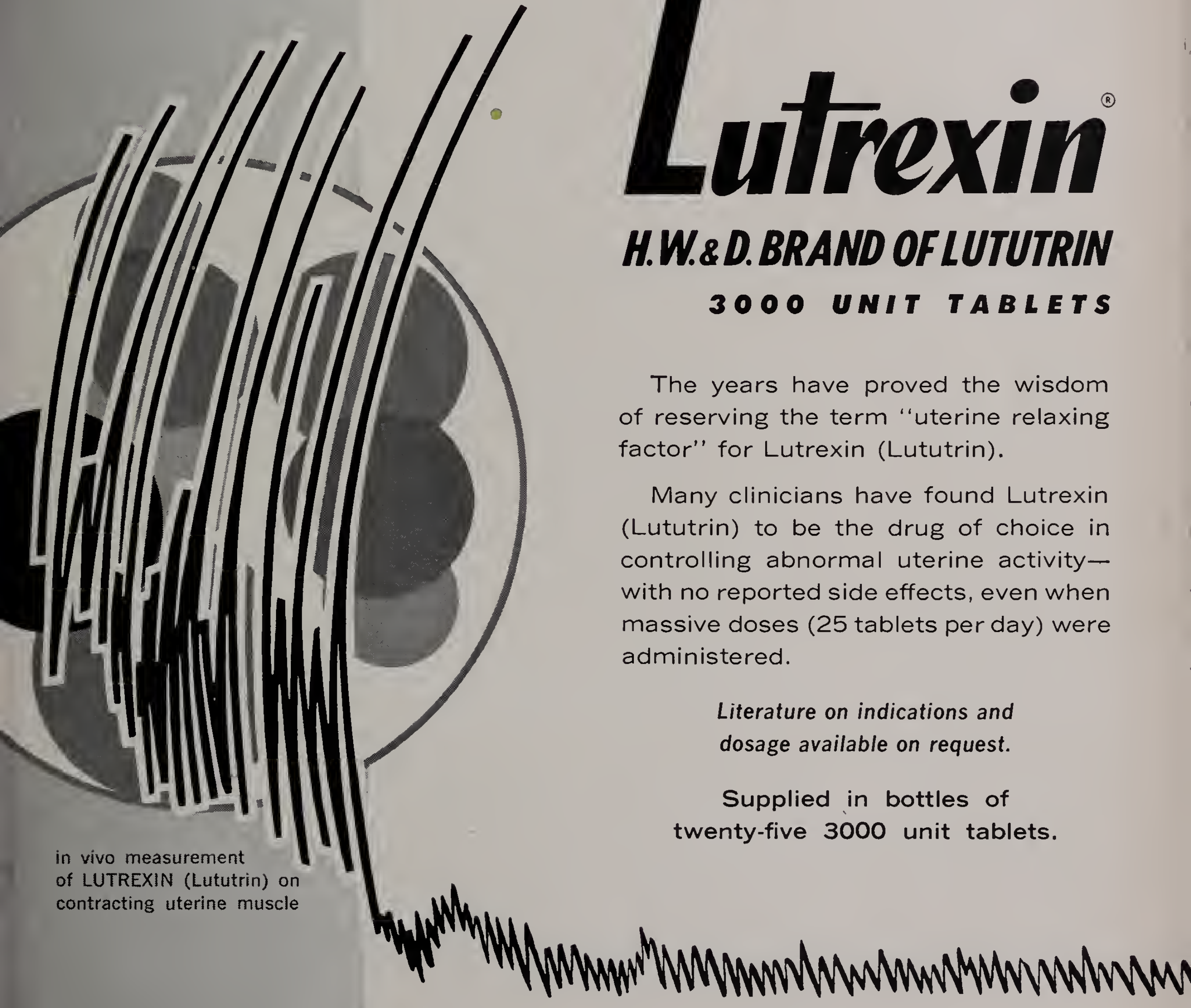

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Number 5

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President's Letter

The editor informs me that if all goes well this issue of *Minnesota Medicine* will be in your hands during early May which gives me the opportunity to discuss the annual meeting of our association in Minneapolis, May 16 to 18. This meeting is always exciting, and this year's program has some features of special interest. On Sunday the sports minded gentry will have their golf and skeet shooting. For those poor souls who are condemned (with their full knowledge and consent) to the smoke-filled halls of the House of Delegates the speaker, Dr. Falls, has arranged for all of the Delegates and any other interested physicians to attend the meeting of the reference committee which will consider the report of the ad hoc committee for the study of Blue Shield. No other reference committee will meet at that time. As I mentioned last month, the activities of Blue Shield in the near future may be of great importance to all practicing physicians. The suggestions for a closer relationship between Minnesota physicians and Minnesota Blue Shield ought to be of interest to all.

This year the scientific sessions will be limited to two full days, on Monday and Tuesday. The schedule presents an enticing mixture of home state talent and authorities from afar speaking on a wide range of subjects. The Academy of General Practice has approved nine hours of credit and, in addition, offers a chance to hear our neighbor, Dr. Donovan Ward speak as the President of the American Medical Association. We are particularly proud to dedicate Tuesday's scientific program to the University of Minnesota Medical School in honor of its 75th Anniversary. The speakers on that day will be alumni or past or present members of the faculty of the University. The banquet on Tuesday evening is an event of recognition and entertainment which no one will want to miss. As usual, the Woman's Auxiliary will help our wives in becoming better informed while they enjoy themselves.

Scientific meetings of state medical societies are not all in a healthy condition. Numerous specialty programs and post-graduate courses offer significant competition. To the credit of Minnesota physicians their attendance in recent years has been respectable, but it should be better. The program committee has not yielded to suggestions that our meeting be confined to a session of the House of Delegates. The scientific and social events and the commercial exhibits will be crisp, interesting, and well worth your time. I hope to see most of you in Minneapolis to meet old friends, make new ones, and gain some new viewpoints.

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The Incidence and Management of Chlorpromazine

Skin-Eye Syndrome*

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WITH THE advent of the phenothiazines in the treatment of the mentally ill, the whole outlook for the psychotic patient has radically changed. Sometimes treatment with these drugs effects prolonged remission of disturbing symptomatology so that patients may function in environments outside the hospital, and sometimes such treatment prevents the mental deterioration that requires prolonged custodial care. The phenothiazines are by no means innocuous drugs. Since their introduction many side effects have been described and studied, some of which are specific to a particular chemical group and some of which are generic to the entire phenothiazine family. Different side effects have variously interested investigators in the ten-year period that these drugs have been used to treat the emotionally ill, and measures to prevent or correct complications have been proposed and tested with varying degrees of success. However, with the use of larger doses and the growth of total length of administration, new and occasionally fatal side effects have appeared. Since very early in the tranquilizer era, those who have prescribed the phenothiazines have been aware of a transitory photosensitivity to sunlight and the subjective complaint of blurred vision in some patients receiving chlorpromazine (thorazine), but both of these side effects have been very easily corrected by discontinuing the drug. The complications recently described, however, comprise changes which do not appear until after years of treatment and seem to be permanent in character.

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Review of Literature

In 1962, French investigators reported, without any discussion of possible physiopathology, a case of facial purplish pigmentation in a patient treated with large doses of chlorpromazine for a number of years.[1] At the beginning of 1964, investigators from the University of British Columbia, Canada, described skin discoloration in conjunction with ocular pigmentation in a series of 70 chronic psychiatric patients at the Provincial Mental Hospital in Essondale.[2] The one thing common to these patients was massive, long-term chlorpromazine therapy.

The skin change consists of a metallic-looking purplish-gray tinge in areas exposed to natural light, principally on the face, neck and forearms. The discoloration may be accompanied by deposits of yellowish-brown pigment in the exposed areas of the conjunctiva, cornea and the anterior central portion of the lens. The ocular deposits can be observed clearly with the slit lamp. The deposits in the skin, which occur mainly in the superficial layers of the dermis and in cells adjacent to the capillaries, can be demonstrated in microscopic sections, where they appear similar to melanin.

A further report described the occurrence of sudden and unexplained death in twelve patients thus affected. At autopsy an accumulation of similar pigment was found in the parenchymal cells of the internal organs.[3] Recently, Satanove has suggested that this complication is due to the phototoxic action of sunlight on the phenothiazine in the skin. The accumulation of melanin and chlorpromazine metabolites may be the cause of the purple color.[4]

Clinical Findings

We in Minnesota became interested in searching for similar cases and have re-

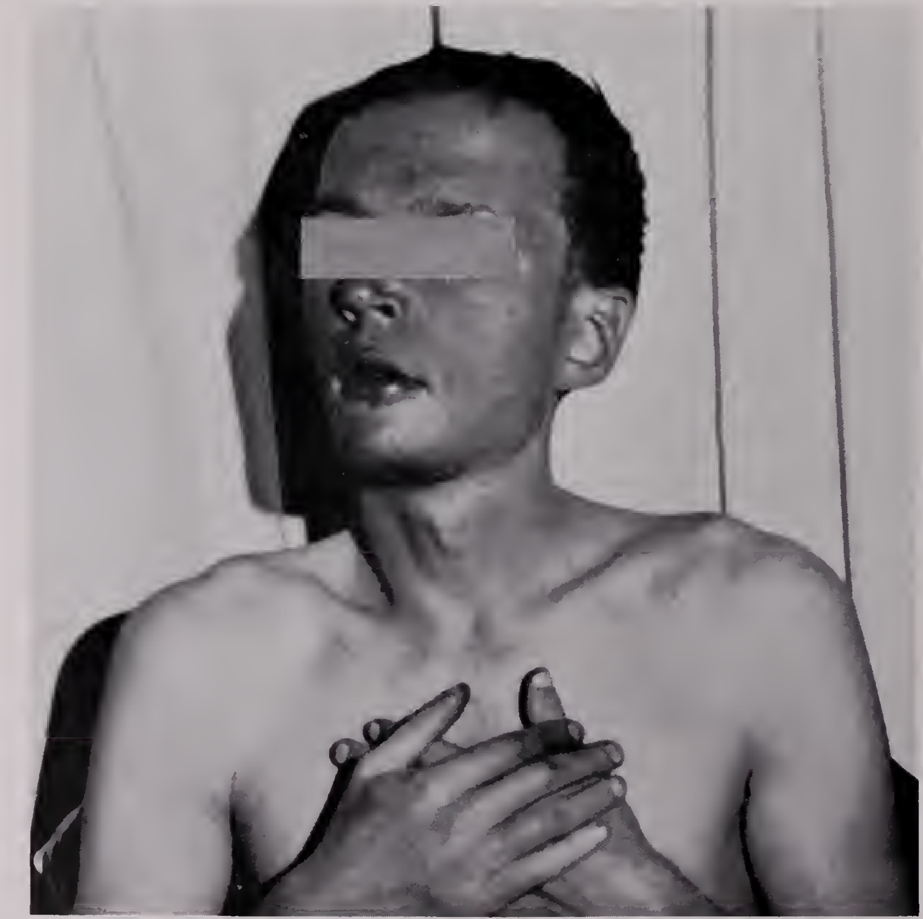

Fig. 1 — Patient 6. Note typical pigmentation on exposed portions of skin.

viewed the populations of two state institutions, where we were able to identify twelve patients who had easily detectable components of the skin-eye syndrome. The dermatologic aspects of some of the cases in our series have already been described in a previous report.[5] The number of patients in both hospitals is around 1700, the cases identified representing 0.7 per cent of the total population. Of the twelve patients (Table 1) found to be affected in our two-hospital population, nine had both eye and skin involvement, one skin involvement only, and two eye involvement only. Figure 1 illustrates a typical case. This photograph was taken in the winter. Conjunctival pigmentation in another patient is shown on the cover of this Journal. Ten patients were female and two male. Ages ranged from 22 to 55 years, and total length of hospitalization from four to 29 years. The physical health of the patients in this sample has been generally good, with the exception of one patient who had tuberculosis in 1947 (later arrested), and one who was treated for anemia in 1960. Visual acuity, where possible to test, was normal except in two patients, one with previous thioridazine-(Mellaril) induced retinopathy** and another with advanced cataract thought to be secondary to chlorpromazine administration. Funduscopic examination was in all cases normal except for the case with the retinopathy. Laboratory data on all patients were essentially normal. Psychiatrically, ten of these patients were classified as schizophrenics, one had psychosis associated with mental deficiency and one had chronic brain syndrome associated with brain trauma.

The total amount of chlorpromazine received by this group varied from 530 gm. to 1890 gm. for periods totaling from three to nine years. Only one patient received more than 1900 gm. of chlorpromazine, but because of a history of confinement at various hospitals it is impossible to state with any accuracy just how much was given; it is estimated, however, that his total dosage was between 2500 and 4000 gm. over approximately seven years of treatment. The highest daily dosage given each patient ranged from

TABLE I

Patient #	Age	Sex	Total Months on Chlorpromazine	Highest Daily Dosage (in mgm.)	Total Amount Received (in gm.)	Involved Areas*
1	40	F	50	2000	1075	E & S
2	40	F	81	1200	1453	E & S
3	28	F	37	1200	545	E & S
4	23	F	35	2000	1158	E & S
5	37	F	60	1600	1042	E & S
6	29	M	±75	5000	±2500 to 4000	E & S
7	38	F	60	2400	1424	E & S
8	55	F	44	2400	533	E & S
9	53	F	95	1600	1893	E & S
10	40†	F	52	1200	1267	S
11	26	M	47	1200	935	E
12	30	F	45	1800	1145	E

*E = eye, S = skin
†At death

TABLE 2

Patient #	Age	Sex	Total Months on Chlorpromazine	Highest Daily Dosage (in mgm.)	Total Amount Received (in gm.)	Involved Areas
1	34	F	69	1600	1059	None
2	55	F	70	1200	1124	None
3	38	M	49	2000	1004	None
4	30	M	35	2000	805	None
5	47	M	46	1200	900	None
6	33	M	43	1200	1293	None

**See Test Your Word Score, page 627.

1200 mgm. to an estimated 5000 mgm.

Searching for patients who had received a similar course of chlorpromazine medication without developing dermatologic or ocular pathology, we were able to find six in the two hospitals. All had received similar total amounts of the drug and similar large daily doses. Their cases are summarized in Table 2. We were thus able to find only eighteen patients in the current two state-hospital population of 1700 patients who had received high dosages of chorpromazine for long periods, and of these eighteen patients, twelve (66 per cent) have developed one or both components of the skin-eye syndrome.

Discussion

A thorough and satisfying explanation of the etiology of skin and eye pigmentation after prolonged administration of chlorpromazine has not yet been put forward. There is very little doubt that chlorpromazine is the drug implicated, as it has been the one consistently administered in all our cases and in those mentioned in the other reports. Although our patients received other phenothiazines, either in combination with chlorpromazine or alone, in no instance were the total amounts administered anywhere near the total amounts of chlorpromazine given, nor did any of these patients receive another drug for periods approaching the length of time they were maintained on chlorpromazine.

It is obviously impossible to predict how much chlorpromazine given for what length of time will produce skin or eye pathology in any given patient. One can only say that these complications appear when large doses are given for extended periods and that the individual patient undoubtedly constitutes the most important variable. This is easily demonstrated by a comparison of Tables 1 and 2, which show that period of administration and total amount of drug received were very similar in both groups and that some patients who developed the syndrome had even received considerably smaller quantities of the drug than some patients who, to all appearances, still have not developed skin or eye changes.

Age was not an apparent factor, as all patients in our series are young or middle-aged adults (22 to 55 years old) and therefore correspond to the age group most likely to have schizophrenia and who are most commonly treated with the phenothiazines in the largest doses for the longest periods. With respect to sex, it is at once apparent that skin and eye pigmentation tends to appear more frequently in females than in males (a ratio of six to one in this series). It is possible to theorize that there could be a deposition of pigment exclusively in internal organs in the patients listed in Table 2, but this is entirely speculative and cannot be demonstrated at the present time. Neither does the appearance of skin or eye pigmentation seem to follow any predictable time sequence. In our sample, previous dermatologic pathology was not predictive that pigment would be deposited in the skin; patients 4, 6, 8, and 12 had known dermatologic trouble in the past (acne, erythematous dermatitis, seborrheic dermatitis), and although patients 4, 6, and 8 later presented skin pigmentation, it has been impossible to demonstrate any skin involvement in patient 12 (Table 1).

Unexplainable sudden deaths among patients with skin and eye pigmentation have been mentioned. There is a similar case in our series. Patient 10 suddenly died after experiencing for 48 hours symptoms consistent with a common cold. This patient was still receiving chlorpromazine, although she had developed skin changes. There had been no noticeable changes in behavior or in mental status, and death was completely unexpected. No signs of homicide, suicide, or struggle of any nature were found. Unfortunately, we cannot give any further findings, since permission for autopsy was denied by her relatives. In the death books of both institutions, from 1960 until the present, we have not been able to find any other case of sudden death which could have been due to similar causes.

The finding of ocular pigmentation without skin involvement in two patients in this series is so far as we know unique in the literature. Since chlorpromazine was discontinued in those two patients, we cannot determine whether they would have later developed skin involvement or if at the time the drug was discontinued any of their internal organs presented pigment deposits.

Management

In all the patients listed in Table 1 (except for patient 10), chlorpromazine has been discontinued and other tranquilizers substituted. These patients have continued to follow their usual routines in the hospital. Patients 1, 2, 3, 4, 6, and 9 have not received chlorpromazine for over six months. In none of them has there been noticeable regression or increase of pigmentation or ocular pathology. Patients 5 and 8 have not taken chlorpromazine for 12 and 17 months, respectively; their conditions are also unchanged. Of the patients listed in Table 2, patients 3, 4, 5, and 6 have continued to take chlorpromazine under close supervision. Examination has as yet failed to demonstrate any pathological changes. Whether such changes will eventually develop is, of course, an open question.

When a patient has been identified as having any component of the skin-eye syndrome, chlorpromazine should be promptly discontinued. In fact, at our present state of knowledge, it might be more prudent to discontinue all psychotropic* drugs and to manage the patient in another manner if at all possible. If the patient continues to be disturbed and needs some type of psychotropic medication, we would recommend a trial with reserpine. In this series, patient 6 had been viciously assaultive for many years, and many attempts at treatment with all forms of therapy, including special management, electroshock, and various drugs, had failed to benefit him. (Note that he had received the largest total dose of chlorpromazine of any of our patients — up to 5000 mgm. a day.) All phenothiazines were discontinued in this patient in May 1964, and he was placed on reserpine in July. At present, his behavior is vastly improved.

If all other treatments fail and the patient remains a difficult management problem, cautious trials with other phenothiazines might be warranted. As yet nothing is known about the possibilities of cross sensitivity, but it seems logical that the more potent compounds of the piperazine class which do not characteristically induce skin reactions and light sensitivity might be tolerated by these patients. Drugs of this type include prochlorperazine (Compazine), trifluoperazine (Stelazine), perphenazine (Trilafon), fluphenazine (Prolixin, Permitil), thiopropazate (Dartal), acetophenazine (Tindal), and carphenazine (Proketazine). It would not seem logical to use the more sedative phenothiazines such as thioridazine (Mellaril), triflupromazine (Vesprin), and promazine (Sparine), which might not be as safe. It might also be well to have affected patients avoid excessive exposure to sunlight, particularly for the first few weeks after chlorpromazine has been discontinued.

Reduction of the abnormal skin and eye changes may become possible through the use of chelating agents. Greiner, Nicolson and Baker[6] in a preliminary report, claim that four out of six pigmented patients improved markedly following a course of treatment with D-penicillamine.

While it is apparent that chlorpromazine is the drug involved in this adverse reaction, we have no assurance that other phenothiazines might not also be capable of producing similar changes. We must keep in mind that chlorpromazine was the first drug to be introduced and has been used in excess of all the other phenothiazines combined.

Conclusion

We have reported on a new side effect of the most widely used and oldest of all the phenothiazines, chlorpromazine. This complication, because of the characteristics of its occurrence, could hardly have been noticed until a relatively short time ago. Our opinion is that the usefulness of chlorpromazine should not be greatly compromised by this new development; however, we would emphasize that closer supervision of patients who have received this agent for prolonged periods is called for, especially when the drug has been given at high doses. Chlorpromazine should always be permanently and promptly discontinued when any sign of skin or eye pigmentation appears. Temporarily withdrawing chlorpromazine for months or even years does not seem to be of any value in preventing eventual occurrence of pigmentation, as most of the patients in the present series were without chlorpromazine for longer or shorter periods in the course of therapy.

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*See Test Your Word Score, page 627.

We feel that even a large total amount of chlorpromazine administered over a long period of time is not sufficient in itself to bring about the skin and eye changes observed, as we were able to compare our series of affected patients with a similar series of patients who had undergone equally long-term, high-dosage therapy with chlorpromazine but who did not demonstrate the same pathology. It appears that other factors, still unknown, but possibly involving differences in metabolic pathways, may be implicated in the production of these complications. With more extensive investigation of the metabolism of chlorpromazine, it may be possible to avoid producing this complication or to treat it after it has developed. For the present, however, close observation and suitable precautions should be the watchwords.

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IT'S THE LAW

Hospital Liable for Pathologist's Misinterpretation of Biopsy — A hospital was held liable for a pathologist's negligent misinterpretation of biopsy material, as a result of which a patient's uterus was unnecessarily removed. The Ohio Supreme Court, in affirming lower court judgments, held that the hospital was estopped* from disclaiming responsibility, since it represented that the pathologist was in its employ as a part of its regular establishment.

The pathologist had a salary contract with the hospital to do pathological work, but he was ostensibly connected with the hospital as an employee. Bills for his services to hospital patients were rendered by the hospital, and his pathological reports were made under the name of the hospital. In the trial court, the jury found him to be an agent, by estoppel, of the hospital.

The high court also ruled that the suit was not barred by the state's one-year statute of limitations on malpractice cases. The statute does not begin to run, the court said, until a medical relationship has finally terminated. In this case, suit was filed more than a year after the patient left the hospital following a hysterectomy performed after the pathologist diagnosed her condition as carcinoma of the cervix. However, she returned to the hospital periodically for cancer checkups, and suit was filed within a year of the final checkup. Moreover, the court ruled, since a hospital may not lawfully practice medicine, the two-year statute of limitations governing ordinary negligence in personal injury cases, rather than the malpractice statute, could be applied in this case.

Lundberg v. Bay View Hospital, 191 N.E. 2d 821 (Ohio, July 3, 1963)
*See Test Your Word Score, page 627.

I ain't no intellectual. — *William Falconer*

Multiple Basal Cell Epithelioma

• Jaw
• Cyst
• Syndrome

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RECENTLY A syndrome has been described in which patients have multiple basal cell epitheliomata and, in addition, cystic lesions in the upper and lower jaws.[1] The skin lesions vary from trichoepitheliomata,* or nodular basal cell lesions, to ulcerative invasive growths. The prominent feature of the skin lesions is the multiplicity of the growths (multiple epitheliomata occurring over a relatively few years) and the occurrence of these malignancies in young persons, often as early as puberty.

The epithelial cysts described are limited to the mandible and maxilla and, though often in close proximity to developing teeth, are not necessarily all dentigerous* cysts.

Other frequent features of this syndrome are bifid ribs, calcification of the dura or falx cerebri, broad nasal root, frontal bossing, spinal scoliosis and cutaneous pits on the hands and feet.[2,3]

The frequent appearance of the basal cell epitheliomata, usually on the face, is the most obvious manifestation, and the jaw lesions are often asymptomatic. In the case presented here, a young man with numerous basal cell epitheliomata of the face was subjected to roentgenographic examination of the facial bones and skull. Two large "dentigerous cysts" were present, one in the mandible and one in the maxilla.

Case Report

A 23-year-old man came under care in September, 1961. One month previously, a basal cell epithelioma had been removed from behind the right ear. At this time a two-centimeter basal cell epithelioma was present in the left eyebrow region. This was excised and the defect repaired by a local rotation skin flap.

In January, 1964, four basal cell epitheliomata (nose, forehead, right lower eyelid, and right eyebrow region) were excised and the wounds closed primarily. In August, 1964, three epitheliomata were removed from the left lower eyelid and the left lateral canthus region.

In August, 1964, roentgenograms of the facial bones, skull and chest were obtained. A large cystic lesion was present in the ascending ramus of the right mandible and another large cyst in the maxilla. Both of these cysts were in close proximity to abnormally located teeth. No spinal scoliosis was present clinically, but the forehead was prominent and the nasal root was markedly widened. Marked frontal bossing was noted on the skull roentgenogram and calcification of the falx cerebri was present. Roentgenographic examination of the chest did not reveal presence of bifid ribs.

The patient stated that his mother had had a facial epithelioma treated by radiation therapy. Because of the reports of familial occurrence of this syndrome, the patient's parents were examined.

His father, age 54, had never had any lesions removed from the facial skin and none were present at this time. There was nothing in the clinical examination to suggest frontal bossing, hypertelorism,* scoliosis, or jaw deformities.

The patient's mother, age 56, had a depressed scar on the cheek from radiation treatment of an epithelioma in 1964. Lesions which clinically appeared to be basal cell epitheliomata were present over the right lateral canthus, left upper lip, and left knee regions. Her forehead was prominent, showed marked bossing, and moderate hypertelorism

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*See Test Your Word Score, page 627.

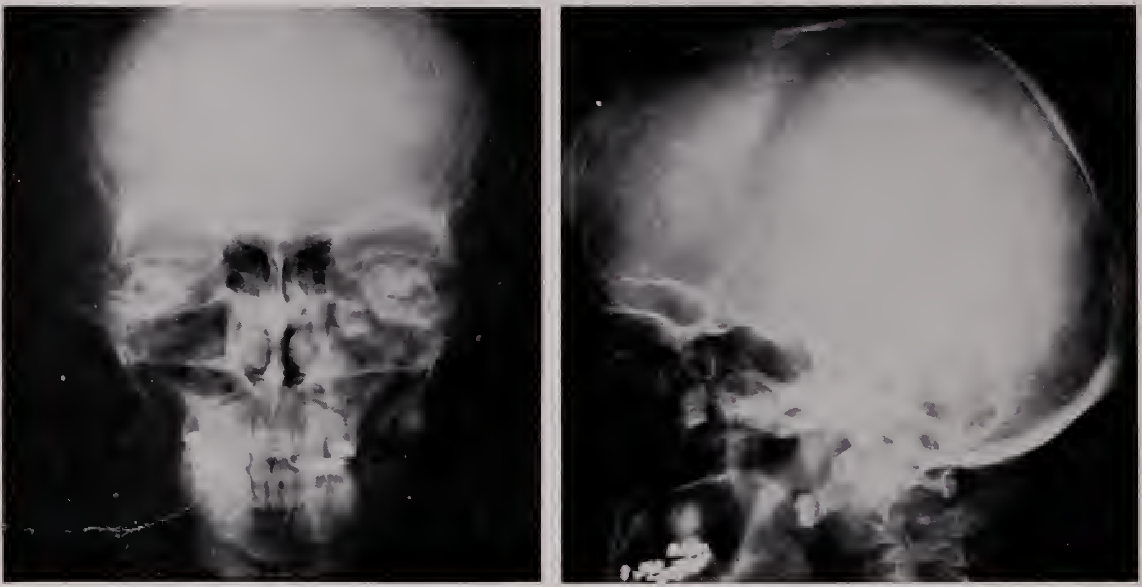

Fig. 1 — Roentgenograms of skull and facial bones showing maxillary and mandibular odontogenic cysts.

was present. No scoliosis or jaw deformities were noted on clinical examination. She gave a history of having a left mandibular jaw cyst treated by marsupialization* eight years previously.

Discussion and Summary

This case is briefly presented to call attention to a recently recognized but not uncommon clinical syndrome. A young patient who, over the past several years, has developed eight distinct basal cell epitheliomata of the facial skin, was found on roentgenographic examination of the facial bones to have two large intraosseous cysts with teeth in close association with them (Figure 1). Other skeletal abnormalities were present and are recorded above. The syndrome was probably also present in his mother.

The cystic masses in the jaws should be removed, or at least observed closely for change in their character. Should these cysts expand to where fracture is likely, or if they appear to be ameloblastomas, they should definitely be removed.

The basal cell epitheliomata of the skin (usually facial) are best managed by plastic surgical techniques. Often they can be simply excised; but occasionally, because of size or location, a free skin graft or a local rotation pedicle skin flap may be needed to repair the defect. Though irradiation therapy will control the individual lesions, it should not be employed once the syndrome is recognized, because of the relatively young age of the patients and the probability that more lesions, possibly dozens, will develop over the ensuing years. The long-term management of the repeated crops of epitheliomata about the face and body can be better handled by surgical means.

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*See Test Your Word Score, page 627.

Drive Safely
Death and dice level all distinctions. — Samuel Foote

Money doesn't make fools of persons, but it tends to show them up. — Herbert Prochnow

Pleural Effusion Associated with Coxsackie Disease*

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THE FIRST clinical syndromes due to Coxsackie viruses were described by Daae and Homann in Norway in 1872,[1] and by Finsen in Iceland in 1874; but the Coxsackie viruses were not isolated until 1948.[2] Finsen called the disease "pleurodynia" because pleural pain was the outstanding feature of the syndrome he described. The first recorded outbreak of pleurodynia in the United States was in Charlottesville, Virginia, in 1888. On that occasion the term "devil's grip" was coined to describe the pleural pain.[3]

The term "Bornholm disease" (after the Danish Island in the Baltic Sea) was first used by Sylvest in his famous monograph written in 1934.[1] Other pseudonymns for epidemic pleurodynia,‡ besides "Bornholm disease" and "devil's grip," are "epidemic muscular rheumatism," "Bamle disease," "epidemic pleuritic pain," and "acute benign dry pleurisy."[4]

It was not until 1948 that Dalldorf and Sickles recovered the causative virus from the stools of two children with paralytic poliomyelitis. The specimens were collected in the village of Coxsackie, New York, on the banks of the Hudson River below Albany.[5] Like poliomyelitis and ECHO viruses, the Coxsackie group are enteroviruses. They are divided into Group A and Group B on the basis of the lesions they produce when injected into suckling mice. Group A viruses produce lesions in skeletal muscle, while viruses of Group B are principally neurotropic. They have been isolated from flies, cockroaches, and mosquitoes.[5] There are

TABLE I
Diseases and Syndromes Due to Coxsackie Viruses

Epidemic Pleurodynia (B)
Myocarditis (B)
Pericarditis (B)
Orchitis (B)
Epididymitis (B) (9)
Acute Respiratory Disease (ARD) (B)
Aseptic Meningitis (A) (B)
Anterior Poliomyelitis (A) (B)
Herpangina (Vesicular Stomatitis) (A)
Gingivostomatitis (A)
Pneumonia (A) (B) (3,10)
Hepatitis (A) (B)
Exanthemata (A) (B)
Acute Viral Peritonitis
Hepatosplenic Syndrome (B) (3)
Pleural Effusion (B)

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‡See Test Your Word Score, page 627.

now 24 Group A and six Group B strains available for classification, numbered B1, B2, etc.[3]

Syndromes Due to Coxsackie Viruses

Of the common syndromes, *Group A viruses* cause herpangina, and *Group B viruses* are recovered in epidemic pleurodynia, aseptic meningitis, pericarditis, and myocarditis. These commoner syndromes often coexist, overlap, and are "complicated" by other symptoms or syndromes.

Table 1 presents a list of syndromes due to Coxsackie viruses noted in a recent perusal of the literature, illustrating the diversity of clinical illnesses due to Coxsackie infection.

Because Coxsackie viruses can be recovered from healthy people at times, acceptable proof of infection due to a Coxsackie virus consists of (1) isolation of the virus from the stool or diseased tissue, and (2) demonstration of a significant rise in antibodies neutralizing the specific (group-type) strain recovered from the stool.[6]

Complications

Epidemic pleurodynia has been "complicated" by *orchitis and myocarditis* in the same patient.[2] It has also been "complicated" by *pericarditis,* and even in 1933, long before epidemic pleurodynia was identified as a Coxsackie virus infection, Bing reported six cases of pericarditis occurring in patients with Bornholm disease.[7] In epidemics of Coxsackie disease, some patients have *pleurodynia,* while others present other syndromes, such as *hepatosplenic syndrome or pneumonitis.*[3] A small summer epidemic (21 isolates in 28 cases) at Walter Reed Hospital resulted in isolation of four types (B2, B3, B4, B5) of Coxsackie B viruses in the same epidemic. The patients had various syndromes (pleurodynia with orchitis, myocarditis, neonatal encephalomyelitis, pericarditis, aseptic meningitis, etc.) as part of the same epidemic. In fact there were ten distinct syndromes in 28 cases, 15 of which were predominantly pleurodynia.[8]

Sizable epidemics of Coxsackie disease have been studied in Shreveport, Louisiana (1948), California (1956), Massachusetts (1957), Toronto (1958), Great Lakes Naval Base (1958), Montreal (1960), and Lind, Washington (1961). In Lind, 142 cases of B2 Coxsackie disease occurred among the 697 townspeople. In this epidemic, there were 22 cases of pleurodynia, seven of orchitis, and three of epididymitis.[9]

While pleural pain is common in Coxsackie infections, pneumonia and pleural effusion are rare.[10] As stated earlier, one of the pseudonyms for pleurodynia is "acute benign *dry* pleurisy," implying that pleural effusion is not seen in this disease, and study of reported outbreaks confirms the notion that pleural effusion is uncommon.

In 1961 there was an extensive outbreak of illness clinically suggesting Coxsackie disease in Nassau County (N.Y.), and the New York State Health Department isolated 84

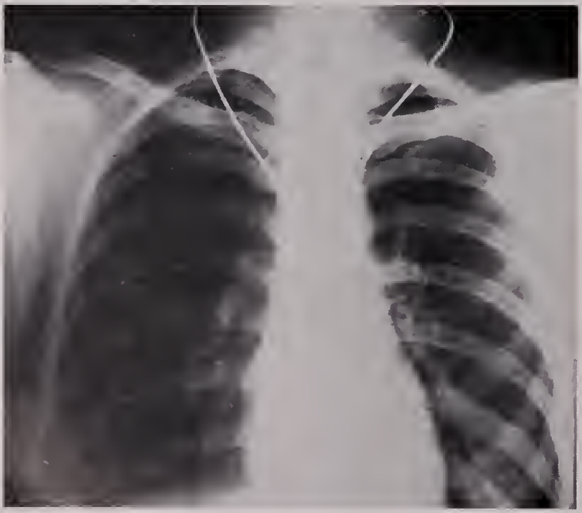

Fig. 1 — (a) PA Chest X ray 7/23/64 negative at onset of illness.

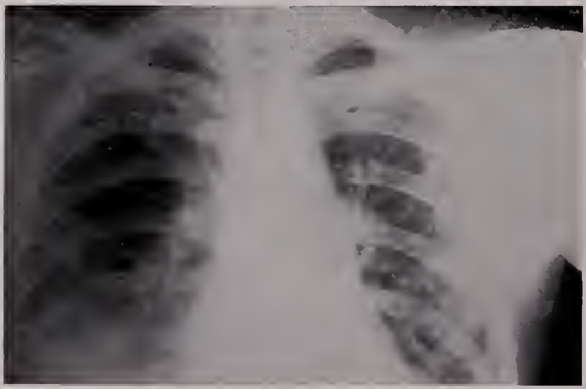

Fig. 1 — (b) PA Chest X ray 8/2/64 demonstrating parenchymal infiltration and pleural effusion at right base.

strains of Coxsackie B5 in 1961; but no cases of pleural effusion were mentioned.[11] In a large (114 cases) epidemic in Boston reported in 1949, a pleural friction rub was heard in 28 cases (25%), but all 98 chest X rays taken were normal.[4] In the Lind, Washington, epidemic of B2 Coxsackie disease, "signs of pleurisy were not found," although 22 patients had pleural pain.[9]

Only three instances of pleural effusion were discovered in an incomplete survey of the recent literature. In the large outbreak (500 cases) in Shasta County, California, in 1956,[1] three cases of pleural effusion were described, all with pericarditis. Coxsackie virus was not isolated in any of these three patients, but two had a significant antibody rise on paired blood specimens. One patient had bilateral pleural effusion, with thoracentesis yielding "275 cc. of thick red fluid."

Because of the rarity of pleural effusion due to Coxsackie disease, the following case is reported:

Case Report

A 23-year-old housewife became ill abruptly on 7/22/64 with severe pain in the epigastric area, in the lower anterior thorax bilaterally, and between the scapulae posteriorly. The chest and epigastric pain was associated with generalized myalgia and fever of 105.4°. She was hospitalized on 7/23/64 for relief of pain and was noted to be "splinting" the thorax. A chest X ray was negative (Fig. 1) and no friction rub was noted. The leukocyte count was 4200/mm.^{3} with a normal differential count. Erythrocyte sedimentation rate (ESR) was 44 mm./hr. The pain and fever relented in a few days without specific therapy, and she was discharged on 7/27/64, feeling well.

TABLE 2
Viral Studies

	7/23/64	8/7/64
Influenza A	Neg.	Neg.
Influenza B	Neg.	Neg.
Adenovirus	Neg.	Neg.
Coxsackie	1:4	1:256

The Coxsackie Serology pertains to Antibodies of B4 Variety Neutralizing the B4 Coxsackie Virus Recovered from the Patient's Stool Collected 7/27/64.

She became ill again on 7/28/64 with chills and fever to 104°, associated with severe pleuritic pain in the right anterior lower thorax. Physical examination disclosed rales and evidence of a right pleural effusion, confirmed by X ray 8/2/64 (Fig. 1). The hospital course was marked by daily fever to 103°, despite administration of penicillin and tetracycline, until 8/7/64, when the fever relented. A repeat chest X ray 8/9/64 showed increase in the right pleural effusion. Thoracentesis of 400 cc. of amber fluid was performed on 8/10/64. An intradermal tuberculin test (O. T. 1:1000) was negative. She was discharged 8/11/64 and gradually gained back weight and strength. Subsequent X rays (9/8/64) still demonstrated pleural disease, at least some of which was effusion on lateral decubitus view (Fig. 1).

Coxsackie B4 virus was isolated from the patient's stool collected on 7/27/64, and a significant rise (1:4 to 1:256) in B4 neutralizing antibodies was demonstrated (Table 2).

Repeat intradermal tests with tuberculin (O. T. 1:1000) and histoplasmin were negative 9/8/64. The following tests were also negative or normal: cold agglutinins, psittacosis complement fixation (CF) test, throat culture, pleural fluid culture, and CF tests for histoplasmosis, blastomycosis, and coccidioidomycosis.

Summary

A case of pleural effusion associated with Coxsackie disease has been reported. The

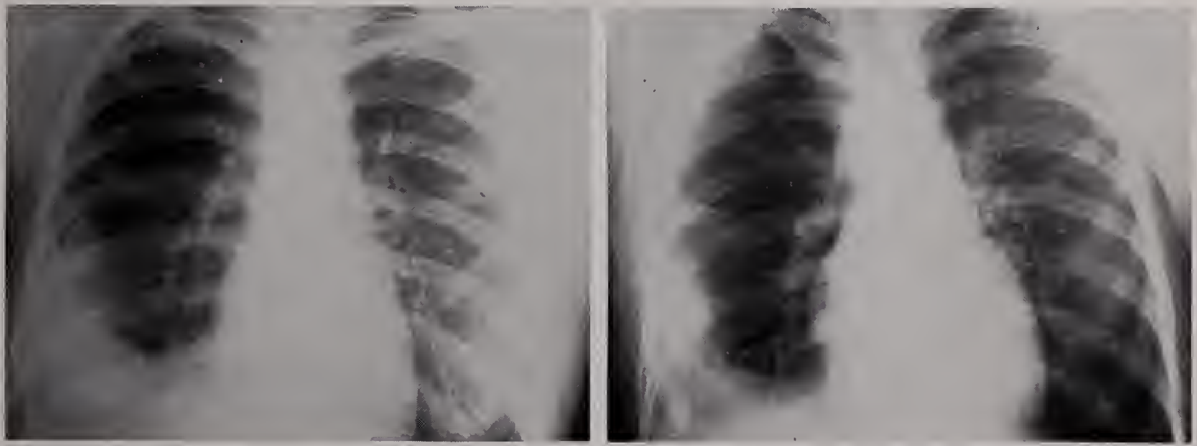

Fig. 1 — (c-left) (d-right) PA and Right Lateral Decubitus Chest X ray 9/8/64 demonstrating free pleural fluid.

Coxsackie virus, Group B, Type 4, was recovered from the stool, and a significant rise in titer of neutralizing antibodies to that virus was demonstrated in the patient's serum at a time when she had a clinical illness characterized by pleurodynia and a large pleural effusion.

A brief review of the history of diseases due to Coxsackie viruses has been included; the diversity of clinical syndromes due to infection with Coxsackie viruses has been described; and the rarity of pleural effusion associated with Coxsackie virus infection has been emphasized.

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FIBRINOGEN — FIBRIN CONVERSION SYNDROME
(Abruptio Placenta Syndrome)

This clinically consists of an abnormal separation of a normally implanted placenta associated with hypofibrinogenemia, hemorrhage and shock. It may occur as often as one in two hundred fifty deliveries.

It is associated with severe abdominal pain which is caused by tetanic contraction of the uterus, and as this occurs there is marked vaginal hemorrhage from incoagulable blood. Shock may supervene.

Hypofibrinogenemia is the result of absorption into the maternal circulation of thromboplastin which causes the fibrinogen fibrin conversion syndrome. Clinical symptoms occur at a level below 150 mg./100 cc. of plasma fibrinogen and the critical level is 90 mg. per cent.

The etiology of this syndrome may be toxemia, hypertension, chronic glomerulonephritis, chronic vascular disease or trauma. It is to be differentiated from placenta praevia in which the bleeding is painless and tetanic contractions of the uterus and the fibrinogen depression are absent.

Energetic treatment is required for abruptio placenta syndrome and the intravenous administration of fibrinogen should be continued until the serum level is well above the critical point of 90 mg. per cent. If this condition is not recognized, prognosis is grave.

Durham — Encyclopedia of Medical Syndromes

In England they believe in ghosts. In America, every family has one in its closet, but we call them skeletons. — C.O.R.

Primary Aldosteronism*

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PRIMARY ALDOSTERONISM, a syndrome of mineralocorticoid excess, was first described by Conn.[1] The classical clinical picture is characterized by hypertension, nocturnal polyuria, intermittent or continuous weakness of skeletal muscles, headache, polydypsia, paresthesias, intermittent "paralyses," and tetany. Laboratory studies show severe hypokalemia, hypernatremia, alkalosis, hyposthenuria, and increased amounts of aldosterone in the urine. Numerous cases[2,3,4] have been described in the literature since the entity was defined. Patients with primary aldosteronism may be asymptomatic, with benign hypertension and hypokalemia being the only clinical abnormalities.

Report of a Case

In May 1963, a 38-year-old woman consulted a physician because of weakness of the legs of one year's duration. Previously the patient had enjoyed good health. The weakness of the legs was so severe that, at times, the patient was forced to crawl up the stairs. At the time of the initial physical examination the blood pressure was 170 mm. Hg systolic and 120 diastolic. An electrocardiogram and a roentgenogram of the thorax were interpreted as normal. The patient entered Miller Hospital on May 13, 1963, for further studies.

During the first hospital admission additional information was obtained from the patient. In the 12 months prior to consulting a physician, she had experienced episodes of dull, aching pain and stiffness in the lower extremities lasting up to one week. The pain was exaggerated by exertion but not by coughing, sneezing, or straining at stool. It migrated from one extremity to the other. The distress ceased during menstruation. In the course of the three months prior to the first admission, the patient had experienced pain in the upper extremities, predominantly in the forearms. During one episode, the arms could not be elevated above the head, because of the severity of the pain. A complaint of tenderness over the radial aspect of the right forearm was elicited. All examiners were impressed by the "hysterical" flavor of the complaints and the apparent indifference to the distress. The result of a Minnesota Multiphasic Personality Inventory was "psychoneurosis, conversion reaction."

No visual difficulty, loss of weight, or intolerance to heat were experienced. The past history revealed that the blood pressure five years prior to admission was 130 mm. Hg systolic and 90 diastolic. Shortly before the first admission, the systolic blood pressure was 190 mm. Hg, and the diastolic varied from 70 to 110 mm. Hg. The patient had not conceived in 20 years of marriage, allegedly because of the husband's infertility. The patient's father was first observed to be hypertensive at the age of 30 years.

Physical Findings

Physical examination revealed a healthy, middle-aged, moderately obese woman in no acute distress. The blood pressure was 160 mm. Hg systolic and 100 diastolic. Funduscopic examination demonstrated Grade I hypertensive changes. The thyroid gland was not enlarged. There was no cardiomegaly; the cardiac rhythm was regular and no murmurs were audible. Palpation of the paraspinous muscles elicited no tenderness or spasm. The cranial nerves functioned normally and the peripheral reflexes were equal bilaterally. There was no detectable muscular weakness or incoordination.

Laboratory Findings

Results of laboratory studies during the first and subsequent admissions are recorded in Tables 1 and 2. Of special interest was the low serum potassium and the low specific gravity of the urine. An intravenous pyelogram performed during the first admission was interpreted as normal.

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Progress

During the first five days of the first admission the patient experienced increasing pain in the calves and slight ataxia. Intravenous administration of 40 mEq. of potassium chloride was followed by an increase in severity of the pain in the legs. The blood pressure remained in the range of 150 mm. Hg systolic and 90 diastolic. The patient was discharged on a program of a weight-reduction diet and orally-administered potassium chloride in doses of one gm. taken three times daily.

Further Evaluation

On June 18, 1963, the patient was admitted for the second time for further evaluation because primary aldosteronism was now suspected. During this admission, a classical history of severe muscular weakness, paresthesias, polydypsia, polyuria, nocturia and tetany was elicited. The patient had not received thiazides at any time. The blood pressure was 140 mm. Hg systolic and 100 diastolic. There was an equivocal Chvostek's sign. The results of the physical examination were otherwise unchanged from those of the initial admission.

Laboratory Data

Several interesting relationships of the laboratory data should be emphasized. The levels of serum potassium varied from 2.2 to 3.2 mEq/L, while the levels of sodium in the serum and the carbon dioxide content of the blood were in the high normal ranges. The excretion of urinary sodium when the patient was maintained on a diet containing 550 mg. of sodium was considerably below the normal of 75-200 mEq/24 hours. The urinary excretion of potassium was within the normal range of 40-80 mEq/24 hours but was considered to be elevated when viewed in the

TABLE I
Summary of Results of Laboratory Study of Constituents of Blood or Serum According to Dates when Studies were Performed

Tests Performed on Blood or Serum	5/10/63	6/19/63	6/20/63	6/27/63*	6/28/63	7/1/63	7/3/63	10/11/64
Hemoglobin (gm./100 ml.)	16.0	14.4	—	—	—	12.9	—	14.6
Leukocyte count (cells/cu. mm.)	9,550	6,050	—	—	—	—	—	7,800
Urea nitrogen (mgm./100 ml.)	13	13	15	—	—	—	—	17
Creatinine (mgm./100 ml.)	1.3	1.6	1.5	—	—	—	—	—
Sodium (mEq/L)	—	143	152	—	135	151	144	141
Potassium (mEq/L)	2.1,2.2	3.0	3.2	3.0	2.5	3.7	3.7	4.0
Chlorides (mEq/L)	—	99	104	—	100	111	106	—
CO_2 content (mEq/L)	—	30	31	—	—	28	29	—
Calcium (mEq/L)	—	—	4.5	—	—	—	4.6	5.0
Phosphorus (mgm./100 ml.)	—	—	2.6	—	—	—	3.0	2.4
Uric acid (mgm./100 ml.)	7.2	6.8	7.1	—	—	—	—	—
Serum cholesterol (mgm./100 ml.)	168	—	—	—	—	—	—	—
Total serum lipid (mgm./100 ml.)	515	—	—	—	—	—	—	—
Fasting sugar (mgm./100 ml.)	89	—	—	—	—	—	—	76
Sedimentation rate (mm./hr.)	15	—	—	—	—	—	—	—

*Day of operation.
—Test not done.

light of the existing hypokalemia. The highest value for the specific gravity of the urine was 1.015. A preoperative electrocardiogram (Fig. 1) showed persistent nonspecific changes of the ST segments and T waves consistent with, but not diagnostic of, hypokalemia. No U wave was apparent.

Surgical Findings

As the clinical picture and results of chemical studies were typical for aldosteronism, surgical exploration was undertaken before the report for excretion of urinary aldosterone was available. During the immediate three-day preoperative period, potassium chloride was administered, the dosage being one gm. given three times daily.

On June 27, 1963, the right adrenal gland was explored using a posterior approach through the bed of the twelfth rib. A yellow tumor, slightly less than 2.0 cm. in diameter, was found in the central portion of the right adrenal gland. The entire gland with the

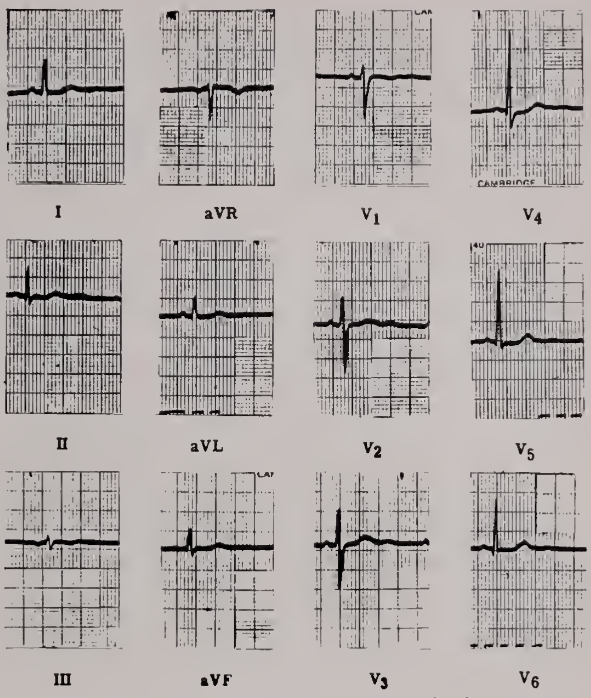

Fig. 1 — Electrocardiogram done during preoperative state.

TABLE 2

Summary of Results of Laboratory Study of Urinary Constituents According to Dates when Studies were Performed

Tests Performed on Urine	5/10/63	6/19/63	6/23/63	6/25/63	6/28/63	7/5/63	10/11/64
pH	6.0	8.0	—	8.0	—	7.0	6.0
Glucose	0	0	—	0	—	0	0
Acetone	—	0	—	—	—	—	—
Protein	0	0	—	0	—	0	0
Specific Gravity	1.006	1.005	1.012, 1.015, 1.013, 1.011, 1.012#	1.007	—	1.015	1.020
Sediment	neg.	neg.	—	neg	—	—	neg.
Catecholamines (ug/100 ml.)	3.0	—	—	—	—	—	0
Sodium (mEq/24 hrs.) (Normal: 75 to 200)	—	25	—	—	80	—	—
Potassium (mEq/24 hrs.) (Normal: 40 to 80)	—	71	—	—	69.2	—	—
Aldosterone (ug/24 hrs.) (Normal: 4 to 32)	—	50.0	—	—	—	—	—
17-hydroxycorticosteroids (mgm./24 hr.) (Normal: 1 to 14)	—	12.7	—	—	—	—	3.9
17-ketosteroids (mgm./24 hr.) (Normal: 5 to 15)	—	16.0	—	—	—	—	7.0

0Qualitative study did not reveal presence of substance.
—Test not done.
#Results of renal concentration test.

contained tumor was removed. The postoperative course was uneventful. Supplementary potassium was not administered postoperatively despite hypokalemia (serum potassium: 2.5 mEq/L) in the first postoperative day. Subsequently, the levels of serum electrolytes reverted to normal ranges. The patient was discharged on the ninth postoperative day.

Clinical Progress

In September 1963, the patient developed increased sensitivity to cold, insomnia, and aching and cramping of the muscles of the legs. In November 1963, nervousness and palpitations were experienced for the first time and occurred once or twice a month. Since spring of 1964, the patient has experienced dull frontal headaches and occasional unilateral sharp, burning cephalgia. Sixteen months after operation (October 11, 1964) symptomatic improvement was equivocal. The patient had always been warm prior to surgery. At no time during the period between operation and re-evaluation had the muscular symptoms become so incapacitating as before operation.

Blood pressure readings obtained periodically during routine office visits in the postoperative period ranged from 140-150 mm. Hg systolic and 100-110 diastolic.

When the patient was admitted for reevaluation, physical examination revealed a blood pressure of 130 mm. Hg systolic and 95 diastolic in the left arm, and 126 mm. Hg systolic and 86 diastolic in the right arm. The respiratory rate was 18 per minute and the pulse rate 76 per minute. There was no significant change in body weight. No abnormal physical findings were observed.

Multiple laboratory studies were done, the results of which were normal. These included a serum potassium level of 4.0 mEq/L. The level of protein-bound iodine was 3.9 ug/100 ml. of serum (normal range, 3.5-7.5 ug/100 ml.). Uptake of I^{131} by the thyroid was 12.4 per cent after 24 hours. The basal metabolic rate was -2 per cent.

The Adrenal Tumor

The pathologic specimen removed at operation (Fig. 2a) consisted of an adrenal gland in the center of which was a discrete, well-circumscribed, bright yellow, homogeneous, 1.8-cm. nodule. Histologically the tumor resembled a typical cortical adenoma (Fig. 2b). The polygonal and hexagonal cells, having clear and lacy cytoplasm, were closely packed. Nuclei were hyperchromatic and exhibited a moderate degree of pleomorphism.* No mitotic figures were identified. The tumor cells were supported by delicate fibrous septae. The structure of the adenoma bore some similarity to that of the zona glomerulosa of the adrenal gland. The adjacent adrenal cortex was atrophic. In sections stained with hematoxylin and eosin, cells in the zona fasciculata and zona reticularis exhibited a deep eosinophilic hue.

Discussion

In all major aspects the case presented represents a classical example of primary aldosteronism. The muscular tetany, polydypsia, polyuria, nocturia, and paresthesias which were present are typical. The degree of hypertension in our case was milder than that in some others reported.[2] Results of laboratory studies typical for this condition included hypokalemia, mild hypernatremia, elevated carbon dioxide content of the blood and a moderate but definite increase in urinary aldosterone. Normal values for urinary 17-hydroxycorticosteroids and 17-ketosteroids were obtained. The electrocardiographic changes were consistent with those of hypokalemia. Our case showed neither the mild proteinuria nor persistently alkaline urine frequently observed by others.

Primary aldosteronism[2] occurs more commonly in the female than the male by a ratio of about 2.5 to 1. Seventy per cent of all cases occur in the fourth and fifth decades of life. Pathologically, 90 per cent of the cases have a unilateral solitary adenoma. Multiple adenomas are observed in the remainder, and in a few of such cases the tumors are bilateral. In the light of these data, the decision in our case to explore the right adrenal gland first was, indeed, fortuitous.

The vast majority (about 80 per cent) of adenomas are small, each weighing less than six gm. and measuring three cm. or less in diameter. Accordingly, it is doubtful whether any roentgenographic studies such as retroperitoneal air insufflation or aortography would delineate many of the tumors which are responsible for aldosteronism. The diagnosis depends on clinical and laboratory information. Since the *sine qua non* for diagnosis is the finding of hypertension and hypokalemia, the clinician should firmly establish the existence of hypokalemia in a hypertensive patient before performing sophisticated and expensive investigative procedures.

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*See Test Your Word Score, page 627.

Levels of free urinary aldosterone are usually, but not invariably, elevated. In cases in which the levels are not elevated, increased levels of derivates of aldosterone (tetrahydroaldosterone) have been detected.[2,5]

Originally, the finding of a benign type of hypertension and hypokalemia afforded an important clue to the diagnosis of primary aldosteronism, but reported experiences indicate that in some cases the hypertension may be of the malignant type.[6] Furthermore, primary malignant hypertension itself may manifest aldosteronuria and hypokalemia. In such cases, there is a tendency for hyponatremia to occur in contrast to the hypernatremia associated with primary aldosteronism.[2]

Conn[2] described a variant of primary aldosteronism called congenital aldosteronism. This condition, which is observed in the first two decades of life, is characterized by the presence of polyuria, polydypsia and hypertension, and by the absence of neuromuscular symptoms. Pathologically, each adrenal gland is hyperplastic.

A point of significance in the differential diagnosis of primary aldosteronism is that it may be simulated by unilateral renal disease.[7-9] Frequently in the latter condition, the 24-hour excretion of protein is markedly elevated in contrast to low grades of proteinuria that characterize primary aldosteronism.[9] Also, the response to sodium restriction may differentiate between the two entities. In subjects with primary aldosteronism, limitation of intake of sodium causes a gradual rise in levels of serum potassium, while in cases of unilateral renal disease the hypokalemia may be unaffected by restriction of intake of sodium.

In recent years a syndrome closely resembling that of primary aldosteronism has been described in the French Literature[10-12] as resulting from excessive ingestion of extract of licorice by "cured" alcoholics who had become addicted to licorice. The signs and symptoms described are as follows: flaccid quadriplegia or quadriparesis, paresthesias, tetany, weakness, polyuria, polydypsia and hypertension. Chvostek's sign was elicited in one case. Laboratory studies reveal a hypokalemic alkalosis, elevated levels of carbon

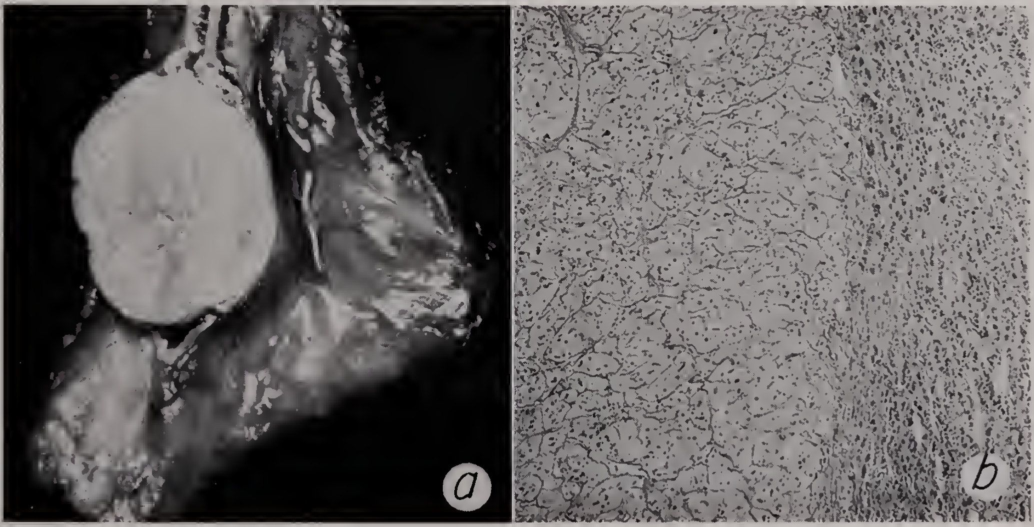

Fig. 2 — Surgically removed right adrenal gland *(a)*. Gross specimen. Cut section of tumor reveals its discrete character. *(b)*. Photomicrograph of junction of the tumor (left side of illustration) and adjacent adrenal gland. Tumor is typically cortical in nature. H & E; x 75.

dioxide in the blood, moderately elevated levels of serum sodium, persistently alkaline urine, and normal urinary 17-ketosteroids and 17-hydroxycorticosteroids. In contrast to primary aldosteronism, the levels of aldosterone in the urine were low. Investigators postulate the close chemical similarity of licorice and DOCA to explain the peculiar biochemical effects. It is doubtful whether clinicians in the United States will have to include this "pseudo-Conn syndrome" in their differential diagnosis.

The basis for a diagnosis of aldosteronism in the case presented seems to be relatively evident. Yet a number of clinical states, such as renal tubular disease,[13] aldosteronism with renal artery stenosis, Cushing's syndrome, and licorice poisoning, must be differentiated from primary aldosteronism. Findings as in the case presented can usually be separated from findings in these other entities by the specific changes noted herein, particularly the normal values for urinary 17-ketosteroids and 17-hydroxycorticosteroids, while the levels for urinary excretion of potassium are high.

Summary

The principal features of primary aldosteronism in a 38-year-old woman included weakness of the lower extremities, paresthesias, polydypsia, polyuria, nocturia, hypertension, hypokalemia, hyposthenuria, elevated levels of aldosterone in the urine and normal urinary levels of 17-hydroxycorticosteroids and 17-ketosteroids.

Treatment consisted of surgical extirpation of the right adrenal gland in which a cortical adenoma was present. Although reevaluation 16 months following operation demonstrated a labile type of hypertension and equivocal symptomatic improvement, the levels of serum electrolytes were normal.

Once medication with thiazides has been excluded, the differential diagnosis includes unilateral renal artery stenosis, Cushing's disease, malignant hypertension, and the excessive ingestion of licorice.

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What counts in knowledge is that which you learn after you reach the point where you know it all. — Advertiser's Digest

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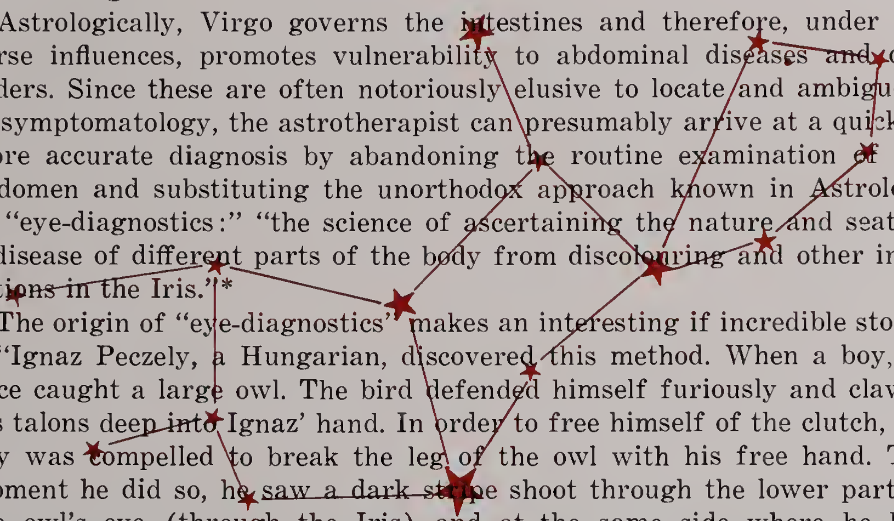
Facts do not cease to exist because they are ignored. — Aldous Huxley

Astrology and Medicine — Virgo, the Virgin

Virgo, sun sign from August 22 to September 22, is visible May evenings in zodiacal transit about midway between the horizon and the zenith, the head and shoulders of the figure near the point where the celestial equator crosses the ecliptic. Virgo represents a virgin holding in her left hand a spike of grain — denoted by the bright 1.2 magnitude star, Spica (spike). In scanning the southern sky after a casual acquaintance with the constellation as delineated on any stellar chart, the interested stargazer is advised to first locate the brilliant Spica and then orient around it from memory the lesser magnitude stars that comprise the total constellation of Virgo.

Astrologically, Virgo governs the intestines and therefore, under adverse influences, promotes vulnerability to abdominal diseases and disorders. Since these are often notoriously elusive to locate and ambiguous in symptomatology, the astrotherapist can presumably arrive at a quicker, more accurate diagnosis by abandoning the routine examination of the abdomen and substituting the unorthodox approach known in Astrology as "eye-diagnostics:" "the science of ascertaining the nature and seat of a disease of different parts of the body from discolouring and other indications in the Iris."*

The origin of "eye-diagnostics" makes an interesting if incredible story: "Ignaz Peczely, a Hungarian, discovered this method. When a boy, he once caught a large owl. The bird defended himself furiously and clawed his talons deep into Ignaz' hand. In order to free himself of the clutch, the boy was compelled to break the leg of the owl with his free hand. The moment he did so, he saw a dark stripe shoot through the lower part of the owl's eye (through the Iris) and at the same side where he had caused the fracture. He dressed the leg, which after some time recovered and he now noticed that according as the process of curing advanced, the dark line became surrounded by a narrow light-colored line, as if it were wrapping the sick place round with a protective layer. This began his research in this line, — which ended in giving quite a new method of diagnostics. Gradually he got to know the exact places in the Iris in which the different parts of the body are indicated by observation of his patients. To the expression "the eye is the mirror of the soul" we may therefore add according to this doctrine, "and of the body."**



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*C. Aq. Libra: Astrology, Its Technics and Ethics. P. Dz. Veen, Amersfoort (The Netherlands), 1917, p. 202.

**Ibid, p. 202-203.

Early Anglo-Saxon Pharmacopeia*

Herbs and plants constituted the chief ingredients in early Anglo-Saxon pharmacology.

Ravens' Leek (a species of orchis): For difficult wounds, take roots of this wort . . . and pound together; it cleanseth the wounds and cures the scars. For sore of eyes, that is, when that one be blear-eyed, take juice of this wort, and smear the eyes therewith; without delay it removes the sore.

Mugwort: For sore of inwards, take the same wort, and pound it to dust, and mix it with new beer; give it to drink, soon it relieves the sore of the inwards. For sore of feet, take the same wort and pound it with lard, lay it to the feet; it removes the soreness of the feet.

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*Payne, Joseph Frank, M.D.: English Med, Clarendon Press, 1904.

Patient Positioning

with an Automatic Bed Positioner

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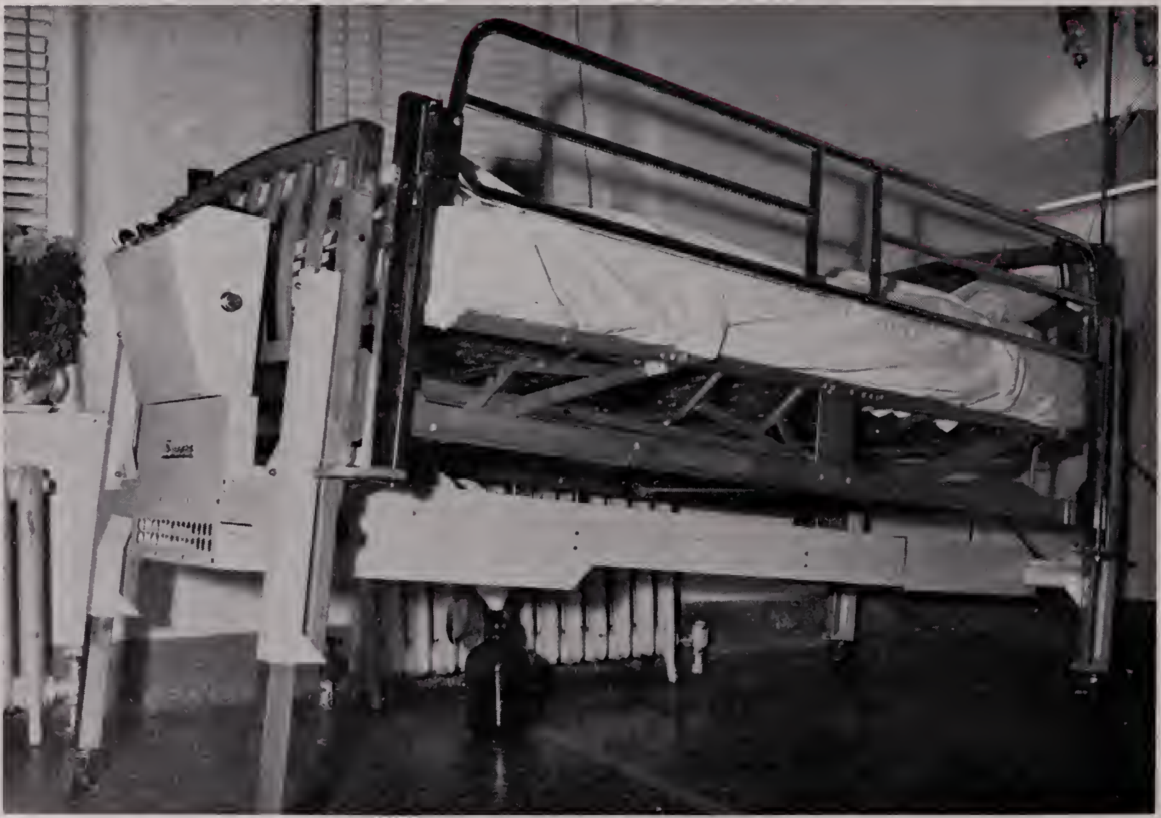

Fig. 1 — Patient positioning.

PRESENT DAY refinements in therapeutic techniques have brought a need for improved management of the bedridden patient from the standpoint of his general body "position." Surgeons usually practice early ambulation of their postoperative patients wherever possible, knowing that postoperative complications are thereby reduced in number and severity. In some medical illnesses, for example those affecting the cardiovascular and pulmonary systems, posture of the patient can be of major therapeutic significance.

The general physiologic "well-being" of bedridden patients has become the principle interest of physiotherapists and specialists in physical medicine. However, the growing number of bedridden elderly patients and seriously traumatized accident victims presents an overwhelming problem from the standpoint of adequate physical therapy during prolonged periods of bed rest. The advent of a new mechanical method to assist in the better and more physiologic care of our patients confined to bed for long periods could be of great value to all groups in medicine. This communication presents a newly conceived device of this kind.

Detrimental Physiologic Effects of Prolonged Sedentary Bed Rest

Normal vigor and healthy tone of body tissues depend on frequent change of position. Prolonged rest of muscle groups leads to a disuse atrophy of muscle cells and supporting structures such as tendons and fascia. Disuse atrophy is commonly found in muscle and other soft tissues as well as in bone in the form of osteoporosis. Factors of repeated stress and strain are important for the health of soft tissues as well as of the skeleton, for tissues add materials necessary for maintenance and growth in answer to the demands of physical stress. Specific physiologic alterations have been shown to result from immobilization of areas of the body with plaster fixation.

Howard et al.[1] and Deitrick et al.[2] have shown that calcium output increases for several weeks and then remains at an increased level in bedridden patients. Nitrogen is also lost, and it can be accepted that calcium and protein are both lost more rapidly from the body under conditions of prolonged immobilization than in normal situations of exercise. It has been shown that the deposition of calcium into the bony matrix is not disturbed, but there is a reduction in the deposit of new protein bone matrix. Under conditions of prolonged immobilization and lack of recurring stress the absorption of mature osteoid continues and a true disuse atrophy results.

Prolonged immobilization is accompanied by an increase in urinary and fecal excretion of calcium. In some studies the calcium content of urine was doubled during immobilization of various portions of the body. Also an increase in excretion of phosphorus, total sulphur, sodium and potassium has been found. As patients begin physical activity during their recovery periods a retention of nitrogen, calcium, phosphorus, sulfur, and potassium has been demonstrated.

Over the years clinicians have learned to recognize the occasional extreme degrees of osteoporosis which are found in chronic invalids bedridden for many months. Ligaments supporting vital internal abdominal organs lose their tensile strength during continued and prolonged recumbent positioning, and even in younger individuals a state of advanced aging of the tissues can be demonstrated. Optimal tensile strength of the connective tissue stroma of the body depends in large measure upon a continual changing stress and strain created by differential tensions between various organs of the body. Over the years there has been ample evidence to support the aphorism that — "As activity decreases, aging increases."

Corrective Measures to Combat the Sequelae of Immobilization

Forearmed with the knowledge that generalized states of osteoporosis and muscle wasting will follow prolonged bed rest it is logical to attempt always a minimum necessary time of complete bed rest. Ordinary and uncomplicated surgical procedures in good risk patients can usually be followed by early ambulation within 36 to 48 hours. Such early mobilization is now considered the "sine qua

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non" for reduction of postoperative complications such as thrombophlebitis, prolonged ileus, atelectasis, and other pulmonary sequelae.

In those situations where patients are confined to bed in traction following trauma or complicated orthopedic surgical procedures, active and vigorous physiotherapy moving all possible joints and muscle groups is helpful. However, in many hospitals the personnel available for physiotherapy are limited in number and restricted in the amount of attention they can direct to a given patient's problem. In lieu of adequate physiotherapy a patient confined to bed for a prolonged period can be constantly changed in position so that the muscle mass of the body moves in a differential relationship to the skeleton at frequent intervals.

Gentle muscle mass and tendon traction on the skeletal system created by a repeated change in position which makes use of differential gravimetric pull can provide effective passive exercise which tends to restore vigor and vitality of the tissues. Unfortunately, in most hospitals such continual movement of a patient must be performed by nursing and ancillary personnel, and such a program is burdensome and incapable of accomplishment with present staffing problems.

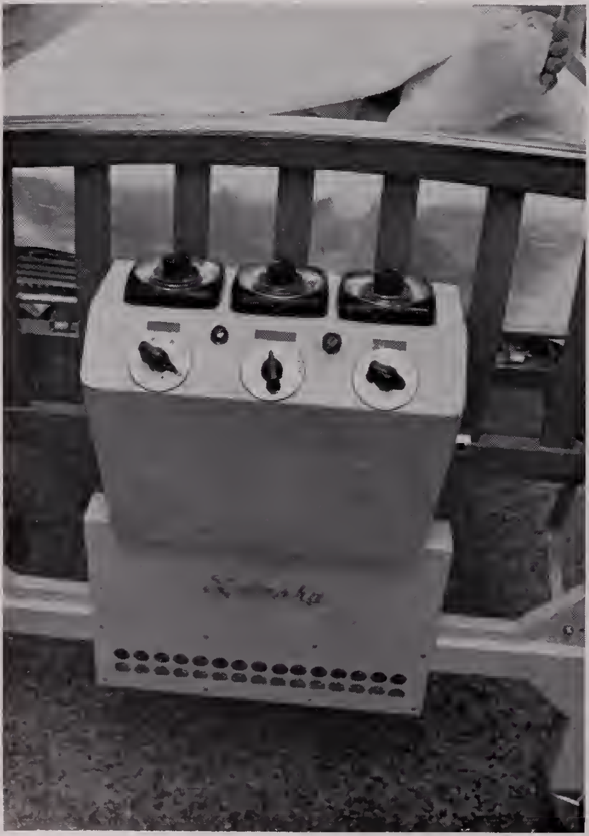

Fig. 2 — Instrument panel.

Previous experience of the author with osteoporotic patients on a rapidly oscillating (poliomyelitis type) bed has shown a remarkable reversal of urinary excretion of calcium with improved ossification of bone.[3] In this experience the negative calcium balance induced by severe skeletal metastases of breast cancer was reversed by the simple expedient of creating a tension between the shifting mass of muscle and the gravimetrically different skeleton. For most patients, however, a vigorously oscillating bed is an annoyance. This paper presents a newly designed and constructed mechanical bed alternator to accomplish this physiologically desirable change of position on a continual basis. Thus, a mechanical device can be utilized to produce a more healthful and physiologically acceptable environment for the bedridden patient.

Versatile Automatic Bed Positioner

This electrically driven unit has been designed for simple placement under a standard hospital bed (Figure 1). Adjustment of the length of the legs of the hospital bed for overall height will permit the mattress of the hospital bed to be at a standard height from the floor or at a somewhat reduced height for easy movement of the patient. The essential feature of this bed positioner is the ability to raise either the head or the foot of the bed independently and in a controlled time sequence. The mechanical system utilizes a quiet two-way motor and a system of ball-bearing pulleys and steel cable for the mechanical connections. During engineering construction of the prototype unit a hydraulic system was found to be too noisy for practicable use.

During elevation of either the head or foot of the bed the height of rise can be adjusted from two inches to twelve inches. Selector dials on the control panel at the foot of the bed are available for choosing the desired height of elevation. A master selection switch permits a choice of alternating a head-elevated and lowered sequence without involvement of the foot of the bed. In a similar manner, the selection switch will permit a foot-rising sequence of the bed which is independent of action of the head of the bed. The third choice in the master selector switch permits an alternation of the head-elevated position with a foot-elevated position.

Three electrical timers are incorporated into the control panel (Figure 2) and permit a choice of time from one-half minute to one hour in any given position. Thus, the head may be elevated to a desired height for a variable period of time, the bed returned to a flat position for a specific period of time, and the feet elevated to a desired height for a variable period of time. This maximum controlled setting is automatically repeated until the shut-off switch is used to stop the action. Through a proper choice of dial settings the following combinations can be achieved:

1. *Elevation of head* alternated with a *flat bed position* for a variable time of elevation and flat position from one-half minute to one hour.
2. *Elevation of the foot* alternating with the *flat position* and with time variable from one-half minute to one hour.
3. The *head-elevated position* can be alternated with a *flat position* which in turn can be immediately alternated with a *foot-elevated position,* and the entire cycle controlled for varying and different periods of time for the head-elevated, foot-elevated, or flat position.
4. With a short time interval of one-half minute for each specific position and an alternation of head elevation with flat bed position with foot elevation a gentle and slow continuous change of position from feet elevated to head elevated can be achieved.

From the foregoing description it is apparent that, for any given position of elevation of either the head or the foot of the bed, the variable factors are the height of the unit and the length of time such an elevation is maintained. Complete selectivity of operation is provided for any desired pattern of motion.

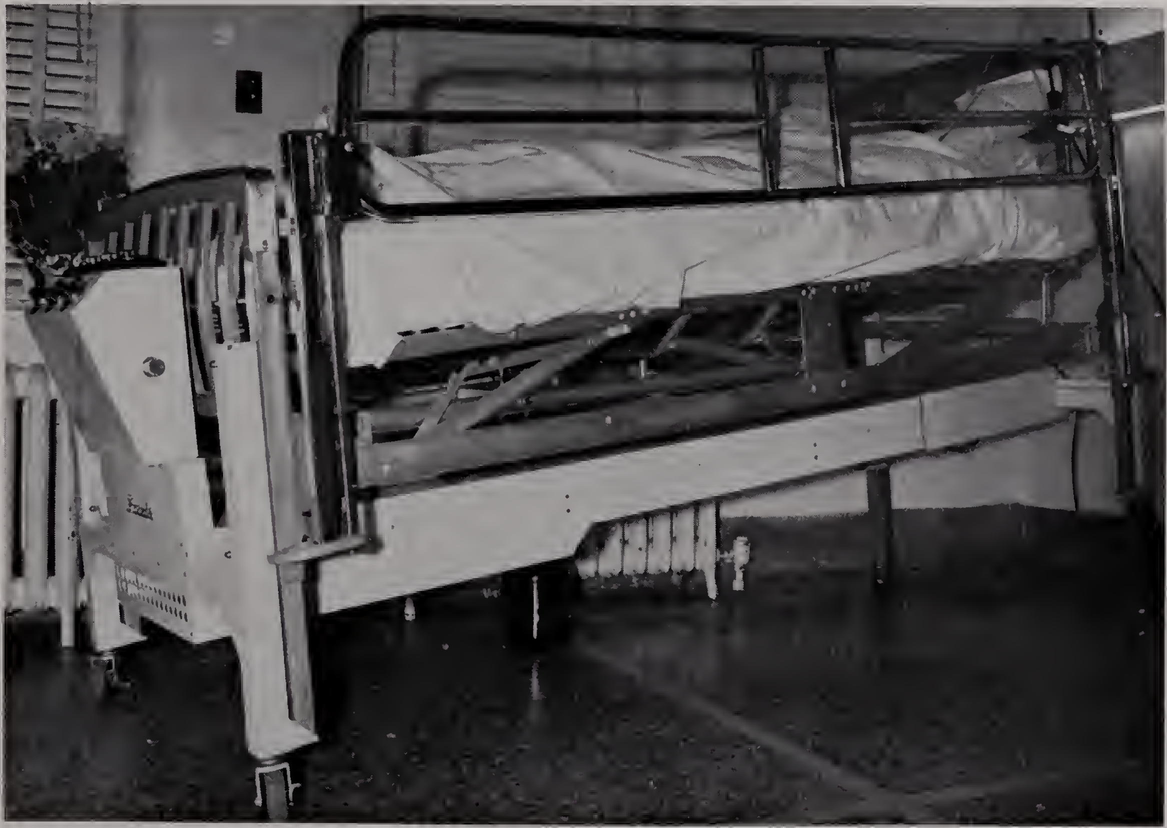

Fig. 2 — Bed positioning.

Standard hospital services are not interfered with, for the unit leaves the area under the patient's bed unencumbered (Figure 3). Suction devices, urine jugs, and other necessary appliances at the bedside can be maintained without difficulty. The alternator unit is mounted on four-inch rubber-tired casters for easy mobility about the hospital. Insulation in the mechanical chamber reduces noise to a barely audible hum. The instrument panel (Figure 2) is mounted at the foot of the bed in a convenient position for operation but without interfering with the sides of the bed. The only requirement for satisfactory operation of the alternator unit is a standard 110-volt electrical outlet.

Application for the Postsurgical Patient

Postsurgical patients who will benefit from a slight Trendelenburg position for a few hours for stabilization of a fluctuating blood pressure can have the foot of the bed elevated to a desired height (two to twelve inches) and for a specific period of time up to one hour. This position can be alternated with a flat bed position or a head-elevated position as desired. A pattern of foot elevation alternated with head elevation in a time sequence of approximately ten minutes for each will reduce the problem of venous pooling in the extremities, will aid venous return to the heart, and will improve pulmonary function periodically.

It is recommended that the head-elevated position be used at a maximum of twelve inches and the foot-elevated position be used at six to eight inches for the routine postoperative patient. During use of the bed positioner all other nursing and supportive functions such as chest catheter suction, nasogastric suction, urinary catheter drainage, biliary tract drainage, etc. can proceed without interference,

Patients Needing Prolonged Bed Rest Following Trauma

Patients confined to bed for prolonged periods in body spicas or extensive plaster casts can benefit from frequent position change. Particularly those patients lying quietly with skeletal traction on both lower extremities as well as upper extremities need a frequent change of the muscle mass relative to the axial skeleton to maintain general body tissue tone. In these situations a constant alternation between maximum head elevation (twelve inches) and maximum foot elevation (twelve inches) with comfortable time intervals at the flat position can provide necessary and beneficial physiologic exercise to the patient. The obvious freedom from attention by nursing and ancillary personnel is noteworthy.

Even with a short-time setting of one-half minute at the head-up or foot-up position the bed positioner function is well tolerated by the patients and they soon become acclimated to the repetitious and frequent body change. Since the standard hospital bed is used, all necessary supporting framework and pulleys for orthopedic skeletal traction can be used indiscriminately. An additional feature in this application is the ability to change the tension and pull of the muscle mass differentially with the skeleton by change of position without interference at any time with the positioning of guy wires for the traction apparatus. Indeed, physiologic bed positioning is achieved with a minimum of disturbance to the patient.

Patients with the Postphlebitic Syndrome

The swelling and chronic edema suffered by the patient following severe deep thrombophlebitis poses many problems in management. Patients of this type benefit greatly from a foot-elevated position for the portions of time when they are at rest. These people should refrain from prolonged sitting in the upright position and should attempt at all times of rest to have their feet elevated slightly above the level of the heart. Commonly, however, these patients are of an older age group and their pulmonary function is compromised slightly by a foot-elevated position if it is prolonged. The use of the automatic bed positioner for ordinary sleep during night hours could achieve both the benefits of the foot-elevated position alternated with the flat or supine position for maintenance of pulmonary health. Only by use of a unit of this kind can such a degree of flexibility be automatically achieved.

Patients with Peripheral Vascular Problems

Older individuals with impaired peripheral circulation frequently benefit from a head-elevated position as they recline in bed. However, venous return is compromised and difficulties from varicose veins and stasis in the peripheral venous bed prevent prolonged dependency of the feet. The use of an automatic bed positioner for alternately raising the head and lowering the bed to a flat position for specific periods of time can greatly improve the management of such difficult cases.

Patients afflicted with venous problems which are aggravated by the dependent position of the lower extremities (varicose veins) are improved when rest is achieved with a mild elevation of the foot of the bed. Pulmonary disease, however, commonly is present and frequent change of position to either a flat or a mild head-elevated position can be helpful. The automatic bed positioner unit can achieve a nicely varied balance for patients of this kind.

Patients with Myocardial Infarction

The patient suffering a myocardial infarction from coronary occlusion commonly does best when treated in a semi-sitting position. However, the general circulation as far as the extremities are concerned benefits from at least a supine positioning or a mild elevation of the feet periodically. Further, such patients who are bedridden for prolonged periods of time would benefit from the differential action of muscle mass on the axial skeleton.

Summary and Conclusions

An automatic bed positioner has been developed to assist patients bedridden for prolonged periods of time and who will benefit from constant change of body position. Shifting of the muscle mass of the body in relation to the axial skeleton has been known to improve the general bone health as well as the general tone of fascia, connective tissue, and muscle mass. Applications for this kind of automatic unit are wide and cover the entire spectrum of disease.

The unit presented has an unusual degree of flexibility and is ideally constructed to be applied to any standard hospital bed. Patients suffering from chronic diseases requiring prolonged hospitalization and bed rest can be more readily maintained in a state of good tissue tone by the use of this kind of automatic positioner.

References

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Charles F. Kettering tells of a friend of his — professor at a famed medical school. Delivering his last lecture on graduating day, he said: "I've been lecturing to you boys on medicine for the last four years — but I'm afraid that half of what I told you is wrong. The trouble is, I don't know which half."

A great part of the happiness of life consists not in fighting battles, but in avoiding them. A masterly retreat is in itself a victory. — Longfellow

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To the wise, life is a problem; to the fool, a solution.

Defeat isn't bitter if you don't swallow it.

Moderate Hypothermia

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THE HAZARD of even temporary complete occlusion of an extracranial carotid artery in adults has long been recognized.

The damaging effect of arteriosclerotic lesions and congenital changes on the collateral pathways in the circle of Willis with extracranial obstruction in addition to this was pointed out by Hunt in 1914.[1] However, it was not until more recently that extracranial thrombotic obstruction of the carotid artery has become associated with the clinical entity of stroke of completed, intermittent or progressive types as described by Gurdjian and Webster in 1953.[2] These authors resected the thrombosed portions of the carotid arteries to effect a sympathectomy of the distal cerebral arterial tree. With this there began to appear reports of the successful surgical treatment of other extracranial carotid and vertebral arterial lesions of aneurysmal[3] and stenotic types in patients[4] with symptoms of cerebral ischemia. Although there was encouraging success in these reports, surgical occlusion of the extracranial carotid arterial system was still accompanied by irreparable brain damage in some instances.

Early in our experience with surgery of the extracranial carotid arteries it became apparent that patients with completed strokes in the acute phase were not, as a rule, candidates for immediate surgery. From 1955 to January 1958, five such patients were operated upon, only one of whom showed improvement.

Although this was a small sample it was decided to reserve carotid surgical treatment for those stroke patients who were recovered and for those with progressive or intermittent cerebral ischemia who might benefit from increasing the cerebral arterial circulation. However, there still remained the possibility of irreversible brain damage in patients during occlusion for repair of a stenotic or compromised carotid artery which represented a critical blood supply to the brain. It was thought that total-body hypothermia might be effective in preventing cerebral damage in these cases.

Rosomoff and Holaday, in 1954,[5] showed in dogs that with each degree centigrade drop in body temperature the cerebral blood flow and oxygen consumption of the brain dropped 6.7%. They found that as long as respiratory and cardiac functions were maintained, no ischemia of the brain would result.

Marshall, Owens and Swan, in 1956,[6]

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*Presented to Minnesota Academy of Medicine, January 13, 1965.

*In Extracranial Carotid Artery Surgery**

TABLE I
Over-all Results Using Moderate Hypothermia Carotid Artery Surgery Requiring Occlusion

Clinical Symptom Type	Worse	No Change	Improved	Expired	Totals
Complete	0	0	4	0	4
Progressive	1	1	6	1	9
Intermittent	0	0	4	0	4
Asymptomatic	0	1	0	0	1
Sub Totals	1	2	14	1	18
Carotid Artery not Opened					
Complete	0	0	1	0	1
Progressive	0	0	0	0	0
Intermittent	0	2	1	0	3
Sub Totals	0	2	2	0	4
Totals	1	4	16	1	22

showed that with total body hypothermia in dogs the entire major and collateral cerebral circulation could be occluded for three times as long as in the normothermic animals without significant brain damage. In that same year Stone, Donnelly and Frobese[7] studied cerebral blood flow and metabolism in three routine surgical patients, using hypothermia of 82.6° F. to 84.8° F. as an anesthetic adjunct prior to surgery. Their findings showed that if shivering were controlled, there resulted a drop in cerebral metabolism of 76% of normal with the reduction of body temperature down to 83° F. Upon this they postulated that the cerebral blood supply could be shut off for three times the accepted 3-minute time length with impunity.

In the treatment of intracranial aneurysm (22 ruptured and one unruptured), Botterell, Lougheed, Scott and VanDewater[8] cooled patients down to 86° F. and temporarily occluded the carotid and vertebral inflow, when possible, for a period of six minutes while the intracranial aneurysm was clipped. There were 19 survivors, in 16 of whom the result was good from the cerebral standpoint.

Selection of Patients for Hypothermia

Based on these studies and on our previous experience with deep hypothermia in cardiovascular cases it was decided that moderate hypothermia should provide some measure of protection without the hazards previously encountered with deep hypothermia. Moderate hypothermia was used then for patients with lesions thought to require occlusion of an artery representing a significant or critical portion of the blood supply to all or a portion of the brain. This included patients who developed signs of acute cerebral ischemia on preoperative trial occlusion of the artery in question; those showing no intracranial crossover from the opposite side on angiographic studies; and patients with frank angiographic occlusions of all carotid or vertebral arteries except the vessel to be repaired or bypassed.

Visualization of collateral vessels smaller than the vertebral arteries in no instance was considered adequate for maintainance of blood supply during carotid occlusion.

Procedure

A total of 42 operations were done on 36 patients, most of whom were in the seventh decade of life. Twenty-two were made hypothermic by use of a cooling blanket, requiring from three to four and one-half hours to get the body temperature down to the 85° F. to 90° F. range. In most instances the cooling was stopped at 90° F., after which the temperature would drift down to around 86° F., when it was thought optimal to proceed with carotid occlusion. In a few patients it was difficult to attain the 86° F. level even after four and one-half hours of hypothermic effect. These were usually thick-set, muscular individuals.

In two of these patients an internal bypass was used. The occlusion times varied from nine to 22 minutes, with the mean occlusion time at 14.2 minutes.

Results

The clinical results in this series are examined principally from the standpoint of evaluating the possible beneficial or deleterious effects of moderate hypothermia and not as an evaluation of extracranial carotid artery surgery alone. The latter is definitely a consideration in our series but not of primary concern in this study except for possible limited comparison.

Four categories suggest themselves as a description of the clinical status at the end of the hospital stay. These categories are "worse," "no change," "improved," and "expired."

In instances where the postoperative state at the time of discharge from the hospital showed any clinical neurological deficit not documented prior to surgery, the condition is described as "worse." The "no change" category includes those patients whose postoperative status after 48 hours was apparently no different from the preoperative condition. In the "improved" group are those patients who were clearly better clinically at the end of their hospital stay, with appreciably fewer or no signs of the neurological deficit present preoperatively. The "expired" group describes only inhospital deaths. There were no operative deaths.

Improved

Table 1 shows the over-all results in patients operated upon under hypothermia. Fourteen of the 18 patients operated upon under hypothermia requiring occlusion showed improvement. In four other patients using moderate hypothermia the carotid artery was not opened, but constricting bands, or kinking, were removed and stenosis relieved at surgery. Two of these showed improvement.

Table 2 shows the results in those patients with carotid artery surgery requiring occlusion in the normothermic state. Of 16 such procedures 10 resulted in improvement.

The over-all results in reparative carotid artery surgery requiring occlusion are shown in Table 3. Of the 34 operations in this group, 24 resulted in improvement.

The over-all results in the entire series are shown in Table 4. Of the 42 procedures, 26 were followed by improvement.

Improved Cerebration

In three patients with progressive mental clouding, memory loss, and loss of affect, there was a remarkable recovery of cerebration to an alert sensorium* with a return of memory function and affect. In two instances the improvement was enhanced with each of two succeeding right and left carotid artery restorations of normal flow.

Uninvolved Carotid Artery

In three instances the carotid artery was found to be uninvolved to any significant degree, despite an angiographic appearance of an arteriosclerotic stenosing lesion. In one

TABLE 2
Results of Carotid Artery Surgery Requiring Occlusion in the Normothermic State

Clinical Symptom Type	Worse	No Change	Improved	Expired	Totals
Complete	0	3	5	3	11
Progressive	0	0	5	0	5
Intermittent	0	0	0	0	0
Totals	0	3	10	3	16

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*See Test Your Word Score, page 627.

of these the carotid was kinked. None of these vessels were opened (Table 1).

Complications

The complications in this series were neurological, cardiac, and hypotensive. They occurred in six patients, some of whom developed neurological complications, others cardiac or postural complications, still others a combination of two.

Neurological

In one patient operated upon under normothermic conditions an *hypoglossal nerve paresis* was noted on the operative side immediately after surgery and was gone in 48 hours. This manifested itself by deviation of the tongue to the operated side and some slight difficulty in swallowing.

In a second patient operated upon under hypothermia a marked, *generalized muscular spasticity* developed on the contralateral side immediately after surgery, as well as an hypoglossal paresis on the operative side. Both of these neurological deficits were gone in 48 hours. This patient was a very muscular 64-year-old white male in whom a temperature of only 89° F. could be reached after four and one-half hours. Because of this an internal shunt was used, but even with this the total occlusion time was 16 minutes. He was found to have occlusion of both vertebral arteries and a marked stenosis of both internal carotids on angiographic studies. After complete recovery from the first operation the patient was subsequently operated upon on the opposite side to provide the safety factor of a collateral circulation. Except for an inability in accurate computation of multidigital problems of even simple types, he was well for three years after his first surgery. This is the one patient listed as "worse" postoperatively. He died nine months after his second carotid surgery.

Postural Hypotension and Neurological Deficit

A 62-year-old white male operated on under normothermic conditions developed a *right-sided weakness with postural hypotension* one week postoperatively. Both of these conditions gradually cleared in another week. No cardiac abnormalities were found. It is interesting to note that throughout this episode one could palpate the internal carotid artery pulsation intrapharyngeally. The patient has been very active for four and one-half years following surgery without any episodes of hypotension or neurological deficit. He still has a palpable intrapharyngeal pulse in the internal carotid.

A second patient, a 72-year-old man, was operated upon under hypothermia at 86.5° F. and developed *a facial weakness* on the operated side which lasted for 24 hours postoperatively. It is interesting that this patient,

TABLE 3
Over-all Results in Reparative Carotid Artery Surgery Requiring Occlusion

Clinical Symptom Type	Worse	No Change	Improved	Expired	Totals
Complete	0	3	9	3	15
Progressive	1	1	11	1	14
Intermittent	0	0	4	0	4
Asymptomatic	0	1	0	0	1
Totals	1	5	24	4	34

TABLE 4
Over-all Results in Carotid Artery Surgery

Clinical Symptom Type	Worse	No Change	Improved	Expired	Totals
Complete	0	6	10	3	19
Progressive	1	1	11	1	14
Intermittent	0	3	5	0	8
Asymptomatic	0	1	0	0	1
Totals	1	11	26	4	42

operated upon for mental obtundity and lethargy, made an excellent symptomatic response but developed a hypotension immediately postoperatively, requiring vasopressor drugs to maintain a systolic blood pressure over 100 millimeters of mercury. This condition persisted for the first 24 hours after surgery, and his facial weakness was noted to disappear concomitantly with his spontaneous maintenance of a normal blood pressure without medication. No evidence of myocardial damage could be found. This patient has been remarkably alert for the past six months since his surgery and has no other neurological deficits.

Cardiac

A 63-year-old white female was operated upon under hypothermia for a cervical-cephalic extension syncope of two months' duration after a left hemiparesis from which she completely recovered. A total right-carotid-artery thrombosis and a marked left-carotid and bilateral vertebral-artery stenosis were found angiographically. Hypothermia was used, and since the temperature was only 89° F. after four and one-half hours and the blood pressure unstable, an internal shunt was used. The total occlusion time was 14 minutes. Postoperatively the patient was apparently recovering nicely without neurological deficit when she was noted to have a left-sided weakness on the fifth postoperative day. This persisted for two days, and on the eighth postoperative day she developed dizziness unrelated to cervical-cephalic extension and was noted to have *atrial fibrillation and electrocardiographic evidence of myocardial ischemia.* The blood pressure, however, remained normal during this period. Both the electrocardiographic picture and the clinical symptoms disappeared with bed rest and cardiac medication over the next few weeks, and the patient was discharged from the hospital asymptomatic. She expired four and one-half months later of what was thought to be a cerebral vascular thrombosis.

Another 51-year-old male operated on under moderate hypothermia suffered a *myocardial infarction and cardiac standstill* six hours postoperatively. He was revived by external cardiac massage and electrical defibrillation. He survived for 12 more days without apparent sequelae, when he again had a cardiac standstill and could not be revived. Post-mortem examination showed massive, old and recent myocardial infarctions. This case represents the only acute or inhospital death among the patients operated upon under moderate hypothermia.

Deaths

In this series there were nine deaths. Four of these occurred while the patients were still hospitalized and five from three months to five years postoperatively.

Hospital Deaths

Of the acute inhospital deaths two were of patients who had carotid embolectomy procedures and both were due to recurrent multiple or generalized embolism: one 24 and the other 48 hours postoperatively as shown at post-mortem examination. The third patient in this group expired 36 hours after surgery and was found on surgical exploration to have a completely thrombosed carotid system from the subclavian origin to the skull. No attempt at reparative surgery was made. On post-mortem examination the thrombosis was found to involve the circle of Willis also. The latter three patients were all operated upon under normothermic conditions.

A fourth patient operated on under moderate hypothermia suffered a myocardial infarction and cardiac standstill and is described above under "cardiac complications."

Late Deaths

Of the late deaths three were thought to be due to intracranial cerebral vascular thrombosis. This was shown by autopsy in one case at four and one-half months. The second patient had the clinical diagnosis made at death four and one-half years postoperatively with no post-mortem examination. The third of these patients, who expired of what was thought to be a cerebral vascular accident 19 months postoperatively, also had no post-mortem examination. It is worthy of note that this is the only patient in the entire series who developed an aneurysmal dilatation of the endarterectomy site, which might possibly have been a source of emboli and secondary intracranial thrombosis. He was also known to have metastatic adenocarcinoma, presumably from a primary lesion in the colon resected before the carotid endarterectomy was done.

A fourth late death occurred three months after surgery. This patient died of a generalized septicemia, meningitis and suppurative myocarditis shown at post-mortem examination.

The fifth late death occurred at nine months after surgery and was thought to be due to an acute coronary insufficiency. This patient had had two episodes of cardiac failure with pulmonary edema within the previous six months prior to his death. No postmortem was obtained.

Discussion

For the most part in the literature the process of selection for surgery is in terms of the clinical symptomatology and physical findings. No differentiation, separation or exclusion on the basis of angiographic patterns is reported for whole groups. For this reason it is difficult and probably invalid to compare our results with those in the literature. Here preselection before surgical consultation or after angiographic studies may represent a major factor in evaluating results. Our patients operated upon under hypothermia may represent patients not given the benefit of surgery in other centers. Certainly we would have turned down many of these if hypothermia had not been available.

The Occlusion Time

A comparison may be made, however, with the results of series in which a comparable range of hypothermia was used and where complete cerebral occlusion was used for the treatment of intracranial aneurysms as reported by Karlsberg and Adams.[9] They found in their series of 54 patients that when occlusions lasted 10 minutes or less, 60% of the patients made a satisfactory recovery. With longer occlusion times only 30% made good recoveries.

Cardiac Risk

There were two instances of cardiac arrests and one of myocardial infarction. The more extensive surgery involved in opening the mediastinum for total root-vessel occlusion certainly could have played a part here. The one instance in our series of myocardial infarction with arrest six hours after surgery could have been precipitated by the hypothermia and anesthesia. This complication must be expected in any series of patients operated upon for lesions of an arteriosclerotic nature. Our prior experience with hypothermia in this range has not been attended by an increased incidence of myocardial infarction or of cardiac standstill. An already compromised coronary circulation may increase myocardial irritability and interfere seriously with myocardial conduction during the hypothermic state. We have found no good evidence to explain any enhancement of the thrombotic process in diseased coronaries, although such predisposition to thrombosis undoubtedly exists under these conditions.

Hypoglossal Nerve Paresis

The complications of temporary hypoglossal nerve paresis is undoubtedly related to retraction of the ansa hypoglossi during surgery. This can probably be avoided in most individuals if enough time and care are taken in making the exposure.

Hypotension

The postural hypotension seen in one of our patients with its concomitant neurological deficit and lack of evidence of myocardial damage is not readily explainable. We have no reasonable explanation for the patient with post-anesthesia hypotension and neurological findings. Conjecture as to etiological bases for these manifestations would lead us into many areas of discussion not appropriate to this report. It is probable in cases like these that the opening of stenotic, extracranial carotid artery lesions may relieve symptoms as long as a normal blood pressure exists; but associated intracranial occlusive disease not otherwise manifest may become symptomatically apparent with even a relative hypotension.

The patient previously described with the postoperative unilateral spasticity undoubtedly suffered some cerebral damage as evidenced by his persistent difficulties with simple computation. Although he recovered clinically and with little evidence of brain damage, it is likely that in such instances there remains appreciable tissue evidence of ischemic damage as shown by the experimental work of Rosomoff.[10] Such a patient may be more susceptible to further ischemic insults because of a functionally critical reduction in the number of remaining brain cells. This is an added reason for opening other stenotic extracranial pathways, as was accomplished by the second procedure on the opposite carotid artery in this patient.

Hypothermia Safety Factor

With the exception of the one death due to myocardial infarction and the patient considered "worse" in the hypothermic group, a comparison of the normothermic and hypothermic groups shows little difference in the results. Assuming that the above mentioned death was due to the hypothermia, the results still show that the hypothermic group of 22 procedures with 16 improved, five unchanged, one worse, and one deceased, compares favorably with the normothermic group of 16 procedures with 10 improved, three unchanged and three deceased. Since the hypothermic group consisted of patients with appreciably greater operative hazard, the results are encouraging. These findings strongly suggest that moderate hypothermia provides a significant safety factor for the patient with a critical preoperative reduction in collateral circulation to the cerebrum.

Summary and Conclusions

The results of 42 operative procedures on the extracranial carotid artery are presented. Twenty-two operations done under moderate hypothermia (86°F.-89°F.) for what was thought to be critical reduction of cerebral blood supply are compared with those procedures in this same series with apparent adequate collateral blood supply done under normothermic conditions.

The results show that moderate hypothermia may have a protective effect on the cerebrum in the patient with a precarious cerebral blood supply when operation requires temporary occlusion of that supply.

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The Penalty of Overweight
Obesity: She had a lot of fat that did not fit. — H. G. Wells

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As much is lost by a card too many as a card too few. — Cervantes

Treatment of Penetrating Chest Injuries

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EXPERIENCE GAINED in wartime with large numbers of penetrating thoracic wounds has resulted in sound recommendations for management of such injuries under war conditions. The situation with regard to chest wounds in civil life is less clear, however. Since there is a difference between war wounds of the thorax and penetrating chest wounds as seen in a civilian population, it is not surprising that military recommendations for management are not wholly applicable to the nonmilitary situation and that there exists a variety of opinions as to how the civilian chest injury should be treated. The material to be reported here is an analysis of the management of a group of such injuries seen at a city-county hospital. Although the number of patients is smaller than in several other series of civilian penetrating chest wounds, the recommendations for treatment based on this analysis seem warranted.

Clinical Material

During the period January 1, 1959, through December 31, 1964, 39 patients with penetrating chest wounds were seen at the Ancker Hospital. All patients who reached the hospital have been included, even if they expired in the Receiving Room. As in other reported series, young males were most often injured. The vital statistics of this group of patients are illustrated in the table. Patients ranged in age from 15 to 72 years with an average of 30.5 years. Only five patients were over 40 years of age.

Males	32
Females	7
Single wounds	34
Multiple wounds	5
Stab wounds	19
Gunshot	18
Falling tree	1
Car accident	1
Living	34
Early dead (12.8%	5

In addition to the chest wounds, eight patients had injury to abdominal viscera; two had upper extremity injuries, and one patient suffered partial section of the spinal cord in addition. The majority of injuries were incurred in altercations or suicide attempts.

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Early Death

Three of the patients were dead within less than an hour after arrival at the hospital, and after all resuscitative efforts had failed. One, with a gunshot wound in the heart, was taken to the Operating Room and died during thoracotomy for repair. A 72-year-old male, with a prior history of heart failure, expired five days after he was stabbed in the right chest. Autopsy demonstrated bilateral pulmonary edema and a myocardial infarct. The stab wound had penetrated the diaphragm and punctured the liver as well.

Treatment

Emergency Procedures

The patients received blood transfusions for volume replacement as needed, analgesics and nerve blocks for pain, and meticulous attention to tracheobronchial toilet to prevent accumulation of secretions and wet lung.[1,2]

Thoracotomy and Chest Tubes

The specific treatment most often followed was closed thoracotomy, placement of chest tubes, and blood replacement. Such therapy was employed for 26 patients with only one death. Tube drainage was utilized for from two to 10 days with an average of 4.2. Surviving patients were hospitalized a minimum of four days and a maximum of seven months. For patients whose only manifestation of injury was hemopneumothorax, including those who developed complications related to it, duration of hospitalization averaged 4.6 days, with a median of 10.

Other Treatment

Four patients with minimal hemopneumothorax were treated by observation only and all survived. Thoracentesis was the treatment employed for this complication in three patients, all of whom survived. Thoracotomy was used three times. One patient with a gunshot wound to the heart died during an attempt at surgical repair. The remaining two treated by thoracotomy survived and were discharged after 10 days and one month, respectively. Eight patients had laparotomies as part of the initial hospital treatment. Seven of these were found to have abdominal viscera injuries.

Complications

Air Embolism

Air embolism resulted from the inadvertent introduction of air into an intravenous tubing in one patient who recovered without residual effects.

Wound Infection

Superficial wound infection occurred in one stab wound which had been sutured. This responded to simple drainage.

Intussusception

Ileocecal intussusception occurred following laparotomy in a 35-year-old female who had been treated for multiple stab wounds of chest and abdomen. She required reoperation and recovered thereafter.

Empyema

A 19-year-old male was admitted with penetrating thoracic wound and flail chest. The unstable chest was treated by tracheotomy and intermittent positive-pressure ventilation by mechanical respirator; the right hemopneumothorax was treated by chest tubes and suction. Because of inadequate control of the flail he developed pulmonary edema and pneumonia, and thereafter a right empyema which required drainage by rib resection.

Clotted Hemothorax

One patient with hemothorax was treated by chest tubes and suction. Because of persistent opacity of the hemothorax he later required thoracotomy for removal of clots and decortication of the lung.

Discussion

Hemopneumothorax as a complication of penetrating chest wounds has been treated principally by repeated thoracenteses in battle injuries, and operative intervention has been reserved for continuing hemorrhage and other complications. Chest tubes have been employed for tension pneumothorax, but their use has not been recommended for treatment of hemopneumothorax because of an increased incidence of complications. The results obtained in World War II and the Korean conflict support these concepts as sound treatment for the combat casualty with hemopneumothorax.[3-13]

Though penetrating chest wounds in a civilian population differ in several important respects from those seen in wartime, it cannot be assumed that the same treatment can be utilized and that the same complications will follow. The agents responsible for the wounds are different; civilian injuries are usually treated without delay and circumstances for treatment are more nearly optimal. The physician who sees the patient initially continues to supervise his care until recovery, and there is usually no need to transport the patient to another facility while he still suffers from hemopneumothorax.

Emergency Thoracotomy

Emergency thoracotomy has an important place in management of penetrating chest wounds and, in fact, increased survival rates in these injuries will depend on its more frequent use, when there is shock unresponsive to blood replacement and when it is apparent that massive hemorrhage is occurring in the chest. However, most surgeons[14-17] are agreed that the majority of hemopneumothoraces from penetrating chest injuries should be treated by closed means, either by repeated thoracentesis to evacuate air and blood or by chest tubes and suction for this purpose.

Repeated Thoracentesis

Surgeons who employ repeated thoracentesis for treatment of hemopneumothorax offer impressive results and a low rate of complications in support of this type of treatment.[14-17] Thus, if other types of treatment are proposed, it must be shown that they possess advantages over thoracentesis, that results are equal or better, that hospitalization is not prolonged, and that incidence of complications is not increased.

Chest Tubes and Suction

Chest tubes and suction possess advantages over repeated thoracentesis for treatment of traumatic hemopneumothorax: Air and blood is rapidly evacuated from the chest, the lung is immediately expanded, and the patient's ventilatory capacity is immediately restored. There is no evidence that immediate expansion of lung increases bleeding into the chest.[18-19-20] It is possible to follow accurately the amount of bleeding from the chest by measurement of drainage, and need for early thoracotomy can be readily determined. The necessity for repeated procedures is eliminated by use of chest tubes. The average period of hospitalization of patients treated by chest tubes for hemopneumothorax in this series compares favorably with that of patients treated by repeated thoracentesis in other series.[14-15]

Thoracotomy

If chest tubes are used for hemopneumothorax, they must be large bore (40-44 F), so that clotting and occlusion do not easily occur. If there is continued bleeding or massive clotted hemothorax, this type of treatment must be abandoned and open thoracotomy utilized instead. Expansion of lung must be achieved rapidly and treatment with tubes discontinued if this does not occur.

Thoracotomy may be indicated for treatment of penetrating chest wounds either immediately or after a short period of observation. Immediate thoracotomy is indicated in patients with penetrating chest wounds and intrathoracic hemorrhage (demonstrated by needle puncture of chest) if: (1) Profound shock shows no response to rapid administration of O-negative blood or other volume expander and the establishment of adequate airway, (2) In precordial wounds no immediate improvement follows pericardiocentesis and volume replacement. Thoracotomy is indicated after a short period devoted to stabilization of the patient who initially responds to resuscitative measures under the following circumstances: (1) X-ray demonstration of massive hemothorax and shifted mediastinum, (2) removal of 1000 ml. or more of blood from chest initially in a patient who continues to demonstrate cardiovascular instability, (3) continued bleeding from chest tubes of 200 ml. or more per hour, (4) with few exceptions, all other precordial wounds, (5) massive air leak and lung collapse indicating tracheal or major bronchial injury, (6) suspected or proven esophageal injury. Modified thoracotomy may also be required occasionally for closure of large chest wall defects. Large foreign bodies, foreign bodies in close proximity to important mediastinal structures, or foreign bodies which cause infection may require thoracotomy for removal. Usually the decision to remove foreign bodies in the thorax does not have to be made on an emergency basis and can be deferred until the patient's general condition is stabilized.

Mortality

The mortality rate of 12.8% of penetrating chest wounds reported here is somewhat higher than that reported in other series.[14,16,17] All patients who reached the hospital have been included, even if they died so rapidly that effective treatment could not be instituted. Had these patients who were moribund on admission been excluded, the mortality rate for penetrating chest wounds in this hospital would be only 2.8 per cent. However, this latter figure represents neither the true risk of these injuries nor the potential for its improvement, since the patients who expire from exsanguination shortly after admission constitute the majority of deaths from penetrating chest wounds in hospitals today. In this series, four of the five deaths were in this category. It is apparent from numerous studies that the mortality rates from all types of injuries, including penetrating chest wounds, are greatest in the first few hours after arrival at the hospital. This means that emergency hospitals must formulate and aggressively utilize plans for resuscitation and initial management of critically injured patients if results are to be improved. During the past six months two patients, both of whom appeared moribund on arrival with massive intrathoracic hemorrhage, were taken directly to the operating room while O-negative blood was being given rapidly. Thoracotomy was carried out, bleeding was arrested, and both survived. It is very doubtful that either would have lived had time been spent to obtain cross-matched blood or in attempts to correct hypovolemia and restore blood pressure to normal prior to operation.

Summary and Conclusions

The treatment of the majority of patients with penetrating chest wounds is fairly satisfactory and the ultimate superiority of chest tubes and suction or repeated thoracentesis as treatment for hemopneumothorax will depend on which of these procedures can be shown to have advantages over the other; but for patients who exsanguinate rapidly, more aggressive treatment with employment of thoracotomy will be necessary if they are to survive.

In a series of 39 penetrating chest wounds seen during a five-year period, five patients died; an over-all mortality rate of 12.8 per cent. Four of these five deaths were due to hemorrhage and occurred within four hours of admission. To improve survival rates in patients with penetrating chest wounds, thoracotomy to arrest hemorrhage will need to be performed more frequently.

For the majority of patients who are not candidates for early thoracotomy, chest tubes and suction are preferable to repeated thoracentesis for treatment of traumatic hemopneumothorax.

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It may be contrary to the laws of nature, but wild oats and old rye produce the same kind of crop. — Religious Telescope

The Treatment of Ulcerative Colitis with Hydrocortisone Alcohol Retention Enemas*

- A Topical and Systemic Anti-inflammatory Agent

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SINCE THE advent of oral and topical steroids, considerable progress has been made in the treatment of idiopathic ulcerative colitis, a disease of unknown etiology. The medical literature records the experiences of a large number of investigators, representative of which is the account of Spencer et al.,[1] who reported 10 years of experience with corticotropin and oral or topical[2] steroids in ulcerative colitis therapy.

In 1956 Truelove[3] pioneered the use of hydrocortisone-free alcohol via rectal drip. He noted rapid symptomatic and sigmoidoscopic improvement in 66 per cent of the patients treated, but biopsy specimens indicated a lag in histologic improvement. This was attributed to a small amount of ethyl alcohol that was used to keep the steroid in solution. On changing to the water-soluble hemisuccinate sodium derivative of hydrocortisone,[4] Truelove obtained normalization of the mucosa that paralleled symptomatic improvement. Subsequent clinical studies led him to recommend combined oral and topical steroid therapy for optimal effect.[5-7] Several others[8-12,19-21] have reported results comparable to those of Truelove; they used hydrocortisone hemisuccinate by rectal drip, as well as hydrocortisone acetate suppositories, depending on the extent of colonic involvement. Matts[8-10] used prednisolone-21-phosphate, and was the first to employ a disposable plastic applicator for ease of self-administration.

Hydrocortisone and its acetate and hemisuccinate esters show varying degrees of absorption when instilled into the distal colon, according to the findings of Nabarro et al.[13]

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*Cortenema by Rowell Laboratories, Baudette, Minnesota.

These investigators found no detectable absorption with a suspension of hydrocortisone acetate, and only slight absorption with a solution of hydrocortisone hemisuccinate sodium. Hydrocortisone alcohol, on the other hand, was absorbed systemically in amounts up to 83 per cent of the administered dose. Patterson[14] and Schwartz[15] confirmed Nabarro's results with the hydrocortisone esters, but Sampson and Brooke[16] and MacDougall[17] more recently have disputed the earlier work and have claimed significant colonic absorption of hydrocortisone hemisuccinate. The latter studies tend to support Liddle,[18] who reported, in 1956, that 26% of a dose of hydrocortisone acetate (suppositories) is absorbed into the blood stream. There seems to be little doubt that these compounds are absorbed to some extent, but the virtual absence of systemic side effects in extensive clinical use suggests that their absorption from the colon is of a low order.

Whether the desirable clinical results obtained with rectally administered hydrocortisone derivatives in ulcerative colitis are due solely to topical effect or to a combination of topical and systemic effects has not been established. It has been shown, however, that difficult cases respond more favorably to combined topical and oral steroids than to either of these routes individually.[2,6,10,12] Therefore it was our feeling that rectally administered hydrocortisone alcohol should be investigated on the premise that its high rate of absorption might obviate the need for separate oral medication. The advantages of hydrocortisone are its availability and economy, and the fact that its usefulness is well-established in the literature.

Materials and Methods

The preparation used in our investigations is a suspension of hydrocortisone alcohol in saline. Methylcellulose is used as a suspending agent, and it is thought that its emollient properties might add a beneficial effect to the medication by soothing the inflamed mucosa and bringing the active ingredient into more intimate contact with the tissues. The suspension has been used in 60-cc. and 90-cc. quantities. The smaller volume is preferable, because it is better retained and covers an adequate area of the colon. We have used a disposable, collapsible plastic container equipped with a lubricated tip for easy insertion into the rectum. The dosage in every case was 100 mg. of hydrocortisone per dosage unit.

Patients were instructed to carefully instill the suspension at bedtime, lying on their left side with the tip of the container directed toward the sacrum to avoid traumatizing the anterior rectal wall. Patients with severe diarrheas were sedated or given paregoric or a commercial preparation of diphenoxylate and atropine (Lomotil) an hour before instillation of the enema. In some cases, it has proved helpful to tape the buttocks together following instillation to aid retention. The importance of retaining the medication, if only for half an hour, was stressed to the patients.

To date, we have used our preparation in over 40 ulcerative colitis patients, all of whom were intractable to the usual medical management, including salicylazosulfapyridine, oral steroids, bland diet, psychotherapy, etc. All of the patients were from private practice, and the series covered a broad spectrum of severity and extent of involvement. Treatment included one retention enema daily for two to six weeks. In the discussion that follows, 20 patients are included. The remaining cases will be reported on later.

Case Reports

The following three cases serve adequately for the entire group.

Case 1 Male, Age 12

Four-year history of recurring bouts of bloody diarrhea and mucous. Has had five exacerbations with the usual treatment of bland diet, salicylazosulfapyridine oral steroids, and psychotherapy. X-ray evidence of "lead-pipe" left colon. Proctoscopic evidence of friable granular mucosa to 25 cm. that bleeds easily with swabbing (chronic ulcerative colitis with exacerbation). Started hydrocortisone alcohol-retention enemas (Cortenema**) once daily, (h. s.) 7-5-63; clinical improvement in two weeks. Proctoscopic return to normal mucosa in five weeks. No exacerbation for one year. Side effects, "sterism."*

Case 2 Male, Age 49

Three-year history of the passage of blood, mucus, and frequent loose stools, with no remissions. X-ray evidence of "serations" of left colonic mucosa. Proctoscopic picture of "pin-point" ulcerations on a granular friable mucosa to 25 cm. Previously treated with bland diet, Azulfidine, oral steroids, etc. Clinical improvement after one week of daily (h.s.) hydrocortisone alcohol-retention enemas.* Proctoscopic return to normal mucosa in four weeks. "Sterism" and mild acne, but no exacerbations in two years.

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*See Test Your Word Score, page 627.

Case 3 Male, Age 19

Involvement of entire colon with ulcerative colitis with three-year history. Exploratory laparotomy July 1959, because of suspected carcinoma of the cecum. Colon left intact because disease was thought to be subsiding; however, he developed recurring bouts of ulcerative colitis which did not respond to the usual form of treatment during the next four years. Started on Cortenema retention enemas 9-18-62, developed considerable evidence of "sterism" within three weeks but was clinically improved within the same period of time. Proctoscopically normal except for granularity in six weeks with every-other-day retention enemas; revealed normal mucosa except for "foot tracks" two months later. No unusual side effects. No recurrence: 18 months' follow-up.

Discussion of Results

A review of the twenty patients treated is given in Table 1. It will be noted that the majority of this group had ulcerative involvement of the left colon; three had total colonic involvement. Many had long-standing disease (six months to 11 years). All of the patients had received the usual conservative treatment without avail. Six had also received "nonabsorbable" steroid retention enemas. Except for two cases involving the entire colon, with failure to retain the enemas and with advance to toxic megacolon, highly satisfactory results were obtained in all. Although it is too early to make a final judgement, there are indications that the periods of remission for many of these patients will exceed the expected. Side effects have been negligible. Four patients developed moon face (" sterism") and three developed mild acne.

Total Colonic Involvement

Of the three who had total colonic involvement, two developed toxic megacolon despite intensive treatment, and were colectomized. One colectomy patient (Case 16, a 55-year-old male) died postoperatively with pulmonary embolism after a very "stormy" course; the second (Case 7, a 28-year-old female) survived total colectomy with ileostomy, after a very complicated postoperative convalescence, and is now well-adjusted to her ileostomy. The third patient with total involvement of the colon (Case 3, a 19-year-old male) was explored because of indistinguishability from carcinoma by X-ray, not confirmed, however, at laparotomy. His colon was left intact because the changes were felt to be reversible. This patient did not respond to oral steroids, salicylazosulfa pyridine, or other medical treatment; but after being placed on hydrocortisone retention enemas, he improved symptomatically in three weeks. When next proctoscoped five weeks after institution of therapy, he presented a normal appearing colonic mucosa.

The two colectomized patients were first seen with fulminating disease and could not retain enemas; they further went on to develop toxic megacolon. Most physicians and surgeons who have had experience with ulcerative colitis recognize this possibility and agree that not every patient can be cured by conservative measures, but that topical and systemic steroids are very worthy of trial. Close observation is imperative, so that corrective surgery can be instituted immediately if irreversible deteriorization seems imminent.

Regional Enteritis

Several of the patients treated (for example, Cases 12 and 14) had regional enteritis. Case 12, who had had a subtotal colectomy and ileal resection with an ileoproctostomy, developed recurrent rectal disease that did not react to the usual treatment. He responded promptly and has remained well for over one year after a four-week period of treatment with hydrocortisone alcohol-retention enemas. Case 14 had a total colectomy and repeated small bowel resections for recurrences. Further disease developed with a stricture of the terminal small bowel. Since she had no further small bowel to spare to the surgeon, hydrocortisone alcohol instillations and tamponades soaked

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*Cortenema by Rowell Laboratories, Baudette, Minnesota.

TABLE I

Name	Age	Sex	Location of Disease	Duration of Disease	Previous Episodes	Prior Treatment and Results	Duration of Treatment and Results Clinical Improvement	Duration of Treatment and Results Proctoscopic Improvement	Duration till Recurrence with Cortenema (Follow up)	Complications and/or Side Effects
1. M. K.	12	M	Lt. colon and sigmoid	4 yrs.	5	Azulf.,* diet, oral steroids	2 wks.	5 wks.	None (1 yr.)	Mild "sterism"
2. G. S.	49	M	Rectum and sigmoid	3+ yrs.	Continuous	Oral steroids Azulfidine, etc.	2 wks.	4 wks.	None (2 yrs.)	"Sterism Mild acne
3. D. J.	19	M	Entire colon	3 yrs.	Continuous	Laparotomy 7-59, diet, Azulf., oral steroids	3 wks.	5 wks.	None (18 mos.)	"Sterism"
4. I. G. S.	42	M	Rectum	9 yrs.	Innumerable	Azulf., oral steroids, etc.	2 wks.	5 wks.	None (2 yrs.)	Mild "sterism"
5. L. M.	17	M	Rectum and sigmoid	1 yr.	3	Oral steroids Nisulfazole supps., etc.	3 wks.	6 wks.	6 mos. exacerbation, stricture rectosigmoid	"Sterism Mild acne
6. D. K.	42	M	Lt. colon	10 yrs.	Innumerable	Azulf., diet, oral steroids, psychotherapy, etc.	10 days	4 wks.	None (1 yr.)	0
7. E. R.	28	F	Entire colon	5 yrs.	7	Azulf., diet, oral steroids, etc.	Developed toxic megacolon; total colectomy		—	Intraperitoneal and wound bleeding, wound infection, etc.
8. M. S.	68	F	Rectum and sigmoid	2 yrs.	3	Azulf., diet, etc.	2 wks.	6 wks.	None (8 mos.)	0
9. A. S.	37	F	Rectum and sigmoid	2 yrs.	5	Azulf., oral steroids, diet, etc.	1 wk.	3 wks.	None (2 yrs.)	"Spastic" colon syndrome
10. S. G.	25	F	Lt. colon	1 yr.	2	Azulf., oral steroids, diet, etc.	2 wks.	4 wks.	None (18 mos.)	0
11. R. J.	24	M	Rectum and sigmoid	6 wks.	1	Azulf., diet	1 wk.	6 wks.	None (18 mos.)	0
12. J. P.	27	M	Regional ileitis colonic involv.	3 yrs.	Chronic	"The works" and subtotal colectomy	2 wks.	5 wks.	None (13 mos.)	"Sterism"
13. M. H.	34	F	Rectum and sigmoid	11 yrs.	6	Psychotherapy, Azulf., oral steroids, etc.	2 wks.	5 wks.	None (18 mos.)	0
14. M. B.	49	F	Regional ileitis with stricture-(after total colectomy & removal of ½ of small bowel)	23 yrs.	—	Azul., diet, psychother., oral steroids	4 wks. (Steroid-soaked tampons used for ileostomy)	4 wks.	—	
15. D. P.	27	F	Rectum and sigmoid	1 yr.	3	Oral steroids	2 wks.	4 wks.	None (1 yr.)	0
16. H. P.	55	M	Entire colon with "toxic megacolon"	6 mos.	1	Oral steroids, etc.	Total colectomy P. O. death Pulm. embolism		—	Toxic megacolon (Could not retain Cortenema)
17. V. R.	56	F	Lt. colon	1 yr.	2	Laparotomy, Azulf., oral steroids, etc.	2 wks.	6 wks.	None (1 yr.)	0
18. T. W.	21	M	Lt. colon	18 mos.	Continuous	Azulf., diet, oral steroids, etc.	3 wks.	6 wks. 75% improved	"Lead pipe" colon to normal	Anorectal syndrome persists and acne
19. J. S.	37	M	Rectal and sigmoid	5 yrs.	Continuous	Azulf., diet, oral steroids	2 wks.	5 wks.	"Lead pipe" sigmoid to normal	"Spastic colon" syndrome
20. V. C.	15	F	Lt. colon	2 yrs.	3	Azulf., diet, psychotherapy	2 wks.	6 wks.	None (18 mos.)	0

*Salicylazosulfapyridine (Azulfidine)

with hydrocortisone solution were tried. Endoscopic evidence of a relented stricture and a fairly normal mucosal pattern were apparent within four weeks.

Prognostic Guides

The chronicity and extent of disease obviously influences the results of treatment. Patients with rectal and sigmoid involvement or even left colon disease, and those with a short duration of disease, responded more quickly clinically and proctoscopically. However, since this medication has considerable systemic absorption, we are becoming increasingly less reluctant to use it in patients whose entire colon is involved with ulcerative colitis. In these cases, we frequently supplement the retention enemas with oral steroids, such as methylprednisolone.

Strictures and pseudopolyposis are not contraindications to treatment; we have seen both return to a normal mucosal pattern. On questioning, most patients stated that they noted clinical improvement within five to seven days; but since all were private patients and we were somewhat reluctant to incur the cost of repeated proctoscopic examinations, most of them were not re-examined until four to five weeks after treatment was started. Earlier proctoscopic examinations no doubt would have confirmed an earlier return to normal mucosa. This will be confirmed in a subsequent group of twenty patients whose charts are currently being reviewed. This group is very similar to the ones already reported here, except that we have not had to resort to surgery in any of them, and have had only one failure with the hydrocortisone retention enema routine.

In view of our results, there is every reason to believe that hydrocortisone alcohol is absorbed to a greater extent than its hemisuccinate derivative which has been used by the other investigators. The occurrence of mild steroid side effects, as well as the highly favorable clinical results in several difficult cases, suggests considerable absorption of the dose administered (100 mg.). It is entirely possible, also, that an enhanced topical effect is provided by more intimate contact with the tissues during the process of absorption.

We are currently instituting blood-level studies in our private practice and at the Minneapolis Veterans Administration Hospital to ascertain the degree of absorption with our particular formulation. At the same time, radioisotopic venous blood studies are in process at the University of Minnesota with reference to the steroid treatment of factitial* proctitis. It is hoped that both of these investigations will shed light on the unsettled question of hydrocortisone absorption from the colon.

Summary and Conclusions

1. An effective and inexpensive agent for the topical and systemic treatment of ulcerative colitis is discussed. Twenty cases refractory to other conservative measures are described.

2. Location and chronicity are influencing factors in remissions, although involvement of the entire colon and long-standing disease are not contraindications to treatment by this method.

3. Considerable systemic absorption is acknowledged—but we believe this enhances the effectiveness.

4. Objective side effects are few.

5. Although we acknowledge no panacea, until something better is advanced we feel that this treatment is safe, efficacious and worthy of trial in most cases of ulcerative colitis.

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*See Test Your Word Score, page 627.

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9-21 may be obtained from the author or the reprints.

WHAT'S YOUR DIAGNOSIS?

A 21-year-old married female was admitted to the hospital with a six-hour history of abdominal pain.

The onset was fairly sudden with pain in the anal area associated with the desire to defecate. Pain was steady with an occasional overlay of crampy pain. An enema, early in the course of the illness, had given relief for an hour or two. The pain then spread to the lower half of the abdomen and gradually to the upper abdomen. When the pain spread to the upper abdomen she experienced some dyspnoea when lying down. Mild nausea was evident, but there was no vomiting.

The past history was essentially noncontributory. The menstrual periods were normal with the last one two weeks previously. There was no known recent infection.

Physical examination revealed no evidence of upper respiratory infection. There was generalized abdominal tenderness, very marked in the lower half of the abdomen, and especially in the lower quadrant of the abdomen. Rebound tenderness was evident in the lower abdomen, but this finding was equivocal in the upper abdomen. No masses were palpable. The pelvic examination was not wholly satisfactory, due to pain and poor cooperation. No masses were identified, but the area of both adnexae was tender with somewhat more tenderness on the left than on the right. The uterus seemed retroverted, and pain was reproduced when the cervix was manipulated.

Temperature was 98.6. Blood pressure 104/60. Pulse 78.

The urine examination was negative for albumin and sugar with one or two red blood cells in a catheterized specimen. Hemoglobin was 13.1. White count was 18,900. Neutrophile 75; lymphocytes 21; bands 4. Chest X ray was negative.

Flat and upright films of the abdomen revealed gas scattered throughout the colon with a small amount of gas in the small bowel. There was no free gas in the peritoneal cavity.

The patient was operated on under the diagnosis of an acute abdomen.

What's Your Diagnosis? Turn to page 678.

If Nature had arranged that husbands and wives should have children alternatively, there would never be more than three in a family. — Laurence Housman

A drunkard is like a whisky bottle, all neck and belly and no head.
— Austin O'Malley

If you confer a benefit, never remember it; if you receive one, never forget it.
— Chilon

Recommended Dosage of Lomotil Liquid to Control Diarrhea

File:✓ Diarrhea

LOMOTIL®

Age	INITIAL LOMOTIL LIQUID DOSAGE*
3-6 mo.	½ tsp. t.i.d. (3 mg.)
6-12 mo.	½ tsp. q.i.d. (4 mg.)
1-2 yr.	½ tsp. 5 times daily (5 mg.)
2-5 yr.	1 tsp. t.i.d. (6 mg.)
5-8 yr.	1 tsp. q.i.d. (8 mg.)
8-12 yr.	1 tsp. 5 times daily (10 mg.)
Adult	2 tsp. 5 times daily (20 mg.) (or 2 tablets q.i.d.)

*Based on 4 cc. per average teaspoonful.

Note: After diarrhea is controlled the initial dosage can usually be reduced to meet the requirements of the individual patient.

LOMOTIL® TABLETS/LIQUID

Each tablet and each 5 cc. of liquid contains:

diphenoxylate hydrochloride ....2.5 mg.
(Warning: May be habit forming)
atropine sulfate ....0.025 mg.

Precautions

Lomotil is an exempt narcotic preparation of very low addictive potential. Recommended dosages should not be exceeded. Lomotil should be used with caution in patients with impaired liver function and in patients taking addicting drugs or barbiturates.

Cautions and Side Effects

Side effects are relatively uncommon but among those reported are gastrointestinal irritation, sedation, dizziness, cutaneous manifestations, restlessness and insomnia.

Lomotil is a brand of diphenoxylate hydrochloride with atropine sulfate; the subtherapeutic amount of atropine is added to discourage deliberate overdosage.

SEARLE *Research in the Service of Medicine*

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understanding... precedes development

The development of chlorothiazide and probenecid were events of major importance, but perhaps even more important for the future was the Renal Research Program by which they were developed. When Merck Sharp & Dohme organized this program in 1943, it was expressing in action some of its basic beliefs about research:

- Many problems connected with renal structure and function were still undefined or unsolved. The Renal Research Program would begin its basic research in some of these problem areas.
- From knowledge thus acquired might come clues to the development of new therapeutic agents of significant value to the physician.

For example, the Renal Research Program put fifteen years into this search before chlorothiazide became available. But because these years had first led to a greater understanding of basic problems, the desired criteria for chlorothiazide existed before the drug was developed.

Along with other research teams at Merck Sharp & Dohme, the Renal Research Program continues to add new understanding of basic problems—understanding which will lead to important new therapeutic agents.

MSD MERCK SHARP & DOHME Division of Merck & Co., Inc., West Point, Pa.

where today's theory is tomorrow's therapy

Editorials

The Fifty Year Club

In the month of May each year the Minnesota Medical Association honors those members, who have been in practice half a century, by election to the *Fifty Year Club*. The group this year receiving a lapel pin signifying this honor, will be listed in the June issue together with a short biography. Minnesota Medicine congratulates this distinguished group of physicians upon their achievements.

The qualifications for election to the Minnesota Medical *Fifty Year Club* are simple but somewhat demanding, since most of the members of the class of 1915 are not now present to receive the award. These are the requirements: The physician must have been a member of the Minnesota Medical Association continuously since 1915; he must have completed the preponderant majority of his practice in the state of Minnesota; and he must be alive to receive the award.

That far off year of 1915 was a year of cataclysmic struggle for world power in Europe. In this, the second year of World War I, the outcome of the war was still very much in doubt, but the shores of Minnesota were far from world conflict. One comes across scant reference to the war in the local medical journals of that time: The St. Paul Medical Journal and the Journal Lancet, which combined the Journal of the Minnesota State Medical Association, was the official organ of the North and South Dakota state medical associations. The latter was a semi-monthly publication. Doctor W. H. Condit noted that his long planned visit to Vienna had to be cancelled, and to his surprise he found that he could find good training in obstetrics and gynecology in New York.

The great struggle in this state in 1915 concerned the affiliation between the Mayo Foundation and the Medical School of the University of Minnesota. There can be no question that the proposal signed by George Vincent, President of the University, Elias P. Lyon Dean of the Medical School, James E. Moore representing the Surgical Department, Jennings Litzenberg OB-GYN, and Richard Beard of the Medical Department rocked the state medical society to its foundations. This committee reported: "The immediate development, with a minimum of cost to the University of a graduate school in medicine, which will stand absolutely alone in the sphere of medical education in America as compassed today and will set the type of graduate instruction for the country at large, is an opportunity not to be put by, and one of which leading medical educators throughout the country are taking full account." The affiliation, of course, was established, although the objections of the medical profession were vociferous, and several prominent faculty members of the Medical School resigned their positions.

1915 was the year of the birth of several important medical institutions. William Rodman, President of the JAMA in 1915 started a new examining board which he called the

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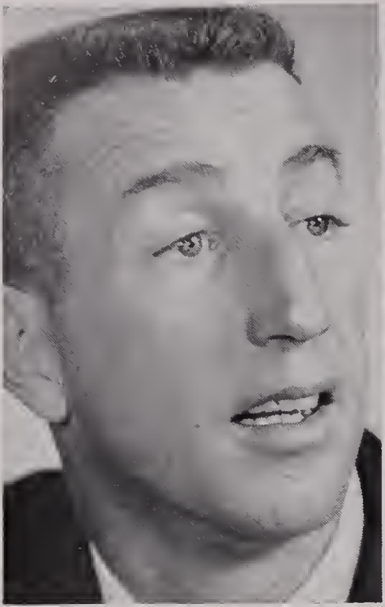
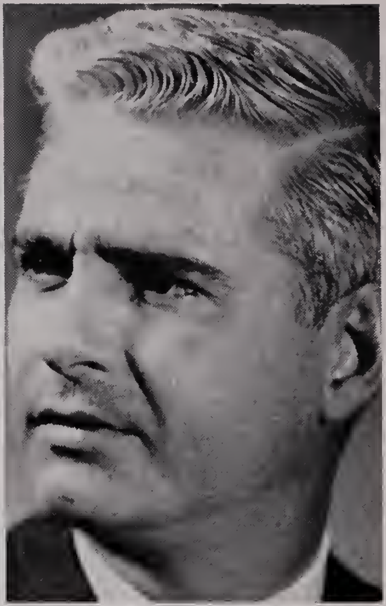


F. P. Tolan, Jr.—St. Paul-Rochester

R. T. Hagenson—Minneapolis-St. Cloud



W. G. Mertes—Minneapolis-Mankato

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National Board, although the first examinations were not given until the following year. The Minnesota Dermatological Society was formed at a preliminary meeting held in Minneapolis, October 19, 1915. Officers for the first year were elected as follows:

President — Burnside Foster, M.D., St. Paul.

Vice President — S. E. Sweitzer, M.D., Minneapolis.

Secretary and Treasurer — G. M. Olson, M.D., Minneapolis.

The following is an excerpt from "Emergency Surgery and Country Practice" by M. M. Grove, Journal Lancet, Volume 35, page 35, 1915.

"Case 3 — Dr. O. O. S., aged 59. For the past several years the patient has suffered from periodic attacks of so-called dyspepsia or indigestion. For the past few months he has lived on malted milk and liquids, any solid food except pancakes producing severe pain in the stomach. The patient had partaken of pancakes three times a day for the past week. About 4 o'clock in the afternoon on October 28, I received a telephone call to go at once to the patient's residence. I found him writhing in pain, retching and gagging. The abdomen was tense and rigid. The pulse rapid and weak. Then upon a hurried but careful physical examination concluded that he had a perforation of the stomach due to an ulcer or malignancy, and I was confirmed in my diagnosis by my colleague, Doctor Eagen. I advised operation at once, but as the patient was one of my own competitors I decided on consultation. Under Ether anesthesia I opened the abdomen through a median incision. On opening the abdomen and bringing the stomach into view, we found a perforated gastric ulcer located anteriorly upon the lesser curvature near the pylorus. The stomach contents, consisting of undigested pancakes, malted milk, and water had poured through the opening in large quantities. The ulcer was not excised but was closed over double suture of linen and then covered with omentum. A posterior gastro-enterostomy was performed, and the appendix removed. The patient made an uneventful recovery. Since the operation he has gained his loss in weight and eats anything and everything."

Excerpt — *The Loyalty of Nurses,* ibid, page 129 by Harriet M. Prime, R.N.

"The advice Doctor George Douglas Head gives to the graduating class of the Asbury Hospital seems very good and very elevating to our profession. But I would like to analyze it to show that it is not quite practical. Because we ask for three hours rest out of the 24 and because we ask for a fixed rate of service, Doctor Head says that our loyalty to high ideals is diminished. A nurse cannot do a duty to a patient if she does not have the proper rest. Doctor Head may say that most patients are not in need of constant attention for more than a few days or a week and that a nurse can stand this for that length of time without rest hours."

Anonymous editorial — "In the past few years an effort has been made to transfuse blood from a normal individual to one who is in immediate danger. Two patients received transfusions of 300 cc and 500 cc without untoward symptoms. The blood from the donor is allowed to run through an ordinary cannula into a glass jar containing 5 cc of a 10 per cent solution of sodium citrate. The combined solution is then poured into an ordinary glass funnel which is connected with the cannula to the patient by means of a rubber tube. The whole process can be accomplished in about 5 minutes."

Item — Journal Lancet, page 275. "Doctor Thomas S. Roberts of Minneapolis has been elected professor of Ornithology and assistant curator of the biological museum of the University of Minnesota. Doctor Roberts is probably the best ornithologist in the Northwest. He will probably some day retire from the practice of medicine, and devote his whole time to University work."

The value of the electrocardiogram in the study of the heart by Ernest T. F. Richards and Ralph E. Morris — St. Paul Medical Journal, Volume 37, page 539: "In the more recent years methods of heart examination and the study of its action have received great impetus through the development of the electrocardiograph. It is coming into use, wherever possible, in all pathological conditions of the heart's action. It is an in-

Continued

What does the association of

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Sanborn Company recently became a division of the Hewlett-Packard Company whose headquarters are in Palo Alto, California. Hewlett-Packard, now in its 25th year, has become one of the world's leading manufacturers of electronic test instruments for government, industry, and research, with plants and sales/service facilities throughout the world. It is still directed by founders Bill Hewlett and Dave Packard and enjoys the widespread respect which their integrity and ingenuity have earned.

SANBORN will now be known as
the
SANBORN DIVISION of HEWLETT-PACKARD.

Sanborn will continue to maintain engineering, manufacturing, sales, and service headquarters in Waltham, Massachusetts. The same intimate knowledge of the instrumentation requirements of the medical profession will continue to guide the management of SANBORN as an H-P Division.

In addition to all that the name SANBORN has meant to doctors over the past 48 years, this new association of SANBORN/HEWLETT-PACKARD means an even stronger organization standing behind every Sanborn instrument and system — stronger in service, facilities, technical knowledge and ability, and in desire to contribute to medical science. Sanborn Division, Hewlett-Packard Company, 175 Wyman Street, Waltham, Mass.

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strument of precision, and through its use the study of cardiac disease has become altered and greatly improved, for the graphic records formed are authentic documents — proofs indeed — of normal or perverted cardiac action."

1915 was a great year for focal infections. Innumerable tonsils were separated from their beds, and dental laboratories were kept busy making plates for patients whose general problems were ascribed to local disease.

This writer, living in the north side of Minneapolis at that time, attending Harrison School across the street from fire engine company No. 16, can recall across the bridge of 50 years the excitement of the fire alarm, the four dappled white horses hitched up in seconds to the steamer and the fine sight of the polished brass and red chariot with the dappled horses, sparks flying from their hoofs and red flames showing in the fire box below the steam generator. 1915 is a year of splendid memories.

Reuben Berman, M.D.
Minneapolis, Minnesota

Hypertension and Renal Artery Stenosis

During the past 10 years, particular attention has been paid to surgical correction of occlusive lesions of the renal arteries in patients with diastolic hypertension. It soon became apparent that renal artery atherosclerosis was quite common among normotensive persons. Indeed, in an unselected necropsy series, we observed[1] moderate or severe narrowing of the renal arteries in 49 per cent of 256 normotensive cases and 77 per cent of 39 hypertensive cases. Clearly, atheromatous narrowing of the renal arteries is not necessarily related causally to associated hypertension. How can we distinguish those cases of hypertension in which the renal artery stenosis is an associated finding from those in which the stenosis causes (or seriously aggravates) the hypertension?

Obstructive lesions of the renal arteries, of diverse cause, may result in altered renal hemodynamics, in changes in the renal handling of solute and water by the individual kidneys, and in the elaboration of pressor substances. The interrelationships between these effects and the production of chronic hypertension in man are not clearly established. However, our studies have indicated that, when there is stenosis of the main renal artery, excellent surgical results may be anticipated if characteristic ipsilateral functional abnormalities can be demonstrated — in particular, the excessive reabsorption of sodium and water and the elaboration of urine having less sodium but more total solute than found in the urine from the contralateral kidney.[2,3] Although renal arteriography and separated renal function studies are the procedures of choice for reliable diagnosis of functionally significant renovascular lesions, operative cost and risk prevent their use in screening large numbers of hypertensive patients.

The procedures which we have found to be of great value in screening include excretory urography (particularly when the technic is modified to include early films) and isotope renography. These tests are safe and easy to perform. Because there is no single uniformly reliable screening test, we carry out both urography and renography in patients suspected to have a renovascular lesion. Very few false-negative results have been encountered. If the tests are positive and if the patient is otherwise a favorable candidate for surgical treatment, further evaluation is carried out by arteriography and separate function studies before operation is advised.[3]

Measurement of pressure gradients may be of value in predicting success in some renovascular lesions, but, generally, these can only be determined at laparotomy, particularly when the stenotic lesions are more distally located. On the other hand, the

Continued

..and in previously treated
ypertensive patients...

Uh-huh.

Regroton improved response
in 76 out of 80...

h-huh.

...reducing mean arterial pressure
from 135 to 112 mm. Hg.

Uh-huh.

on't you even want to try it, Doctor?

I've *already* got eleven patients
doing fine on Regroton.

Why didn't you say so in the
first place?

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in 76 of 80 patients in a 2-year study*

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ɪmposition: Each tablet contains chlorthalidone, mg., and reserpine, 0.25 mg.
ɪntraindications: History of mental depression, persensitivity, and most cases of severe renal hepatic diseases.
ɜrning: Discontinue 2 weeks before general esthesia, 1 week before electroshock therapy, d if depression or peptic ulcer occurs.
ɜcautions: Reduce dosage of concomitant anti-pertensive agents by one-half. Discontinue if BUN rises or liver dysfunction is aggravated. ɜctrolyte imbalance and potassium depletion ɪy occur; take particular care in cirrhosis or severe ischemic heart disease, and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended. Use with caution in patients with ulcerative colitis, gallstones, or bronchial asthma.
Side Effects: Nausea, vomiting, diarrhea, muscle cramps, headaches and dizziness. Potential side effects include angina pectoris, anxiety, depression, drowsiness, hyperglycemia, hyperuricemia, lassitude, leukopenia, nasal stuffiness, nightmare, purpura, urticaria, and weakness.
For full details, see the complete prescribing information.

Average Dosage: One tablet daily with breakfast.
Availability: Bottles of 100 and 1000 tablets.

*Chupkovich, V.; Finnerty, F. A., Jr., and Kakaviatos, N.: The value of chlorthalidone plus reserpine in moderately severe and severe hypertension: A two year study. Presented at the 7th Inter-American Congress of Cardiology, Montreal, June 14–19, 1964.

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significance of a gradient (or its absence) may be greatly reduced because of technical reasons — for example, in lesions of small accessory arteries or with extensive fibromuscular dysplasia.[4]

Another approach to this problem of stenosis and high blood pressure has been based on the possibility of a humoral mechanism. Tigerstedt and Bergman,[5] in 1898, observed pressor effects from renal venous blood and proposed the term "renin." The wealth of subsequent researches into renin-angiotensin-aldosterone mechanisms has helped to explain many experimental types of hypertension, but it has been so diffcult to measure these substances that there has been little practical clinical application of these findings.[6] Indirect assessment of the humoral mechanism, by the measurement of the pressor response to infusion of exogenous angiotensin, has been shown recently to be of clinical value in *carefully selected* instances; patients with functionally significant renovascular hypertension were more resistant to the pressor effects of angiotensin when they did not have malignant hypertension, salt retention states, and depletion of plasma volume.[7] In an earlier study, the angiotensin skin test proved to be a nonspecific reaction.[8] It seems improbable that so complicated a syndrome as renal hypertension will be explainable on the basis of a single mechanism or through the action of a single substance. More likely, angiotensin is but one of many important and interrelated components of a vast but normally equilibrated system whose basic purpose is to provide for the constantly changing requirements of tissue perfusion.[9]

Our first 62 surgically treated patients were selected on the basis of both functional and anatomic criteria, and 40 of them are normotensive six months to five years after operation, 12 are normotensive by the use of only mild to moderately potent antihypertensive agents, and 10 are not improved. Those patients who did not respond well to surgical treatment generally had lesions which could not be satisfactorily corrected from a technical standpoint or did not have clear evidence of a functionally significant lesion.[3]

Although recent researches in the humoral mechanisms of this type of hypertension hold forth the promise of more specific guides to enable the clinician to recognize more easily those patients with surgically reversible renovascular hypertension, our experience indicates that, for the present, both renal arteriography and measurement of function of the individual kidneys are essential to determine the relationship of renal artery stenosis to associated hypertension. In spite of impressive research progress, the management of these patients remains based on enlightened empiricism.

Sheldon G. Sheps, M.D.*
Rochester, Minnesota

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*From the Section of Medicine, Mayo Clinic and Mayo Foundation.

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Smoking and Health

THE ARTICLE "Smoking Habits and Disease in Minnesota," appearing in the January issue of MINNESOTA MEDICINE,* serves as one more reminder that cigarette smoking is a serious health hazard. The responsible physician should be aware of this fact and should act accordingly. As Dr. Luther Terry, Surgeon General of the U. S. Public Health Service, has stated, "None of us should be misled by the half-truth that we need more research before we take action. We need more research . . . but the research is to learn how cigarette smoking produces lung cancer, bronchitis and other diseases, not whether it produces them. On that part of the question, the facts are now in." Indeed, they are!

Certainly, the physician has an obligation to educate the public, and the youth in particular, to the dangers of continued cigarette smoking. We should, by word and example, encourage the heavy smoker to stop and discourage the nonsmoker from taking up the habit.

In addition, the physician has a definite responsibility to those who smoke heavily but who either cannot or will not change their smoking habits. These are the persons in whom there is a distinctly increased risk of lung cancer, bronchitis, emphysema, and heart disease. For example, it is known that in the man who habitually smokes two packages of cigarettes a day, the chance that lung cancer will develop is approximately one in 10.

The chronic cigarette smoker who continues the habit should be advised to have frequent examinations, at least as often as every six months. The examination should include a roentgenogram of the thorax, as well as whatever additional procedures are judged appropriate. In this way earlier diagnosis and, hopefully, more effective treatment of diseases related to smoking may be possible.

Robert S. Fontana, M.D.
Rochester, Minnesota

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Finnagle's Laws

FINNAGLE IS most often remembered for his description of the peculiar properties of the Finnagle factor. In its simplest form the Finnagle factor is expressed as that factor plus or minus which, times which, or divided by which the wrong answer gives the right answer. Application of one or more of the four operations, singularly or in succession will always yield the correct answer to any problem. This factor has been used most often in sophisticated scientific work where the answer to a problem has been less important than the recovery of consistent data.

Finnagle's First Law

"If anything can go wrong it will." A recent study of this law has shown that no continuous function could possibly account for things going wrong. It was apparent, therefore, that such characteristics were quantized in accordance with Planck's laws of quantum mechanics. This work has lead to the restatement called the quantization provision or Murphy's law, which is, everything goes wrong all at once. A further application

Continued

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diperodon 1.0%; oxyquinoline benzoate 0.1% in a special ointment base.

INDICATIONS:
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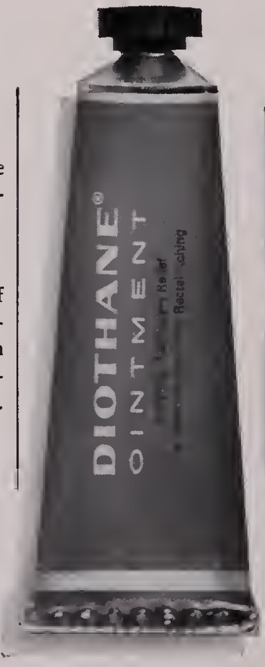

CHILL
↑PULL APART↑

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Provide for temporary palliation of pain caused by hemorrhoids and pruritus ani.

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has been called the Step Ahead principle which is a qualitative measurement of the increasing complexity of the work, the more that is accomplished. The statement of this principle is called Stock-Mayer's theorem after the man who first stated it in the following form- "If it looks easy it's tough; if it looks tough it's impossible."

Finnagle's Second Law

"Matter will be damaged in direct proportion to its value." Strang has attempted to quantitate this law in terms of Strang's misery units. These have been irreverently known as UGS. He has been having trouble though, and so far the base units have not been clearly and inevocably defined. In his studies he refers to the mechanical application of the law: a car that runs smoothly until miles from any garage; the appliance that operates perfectly only when a repairman is there; and the immediate breakdown of anything a day after the manufacturer's guarantee runs out. He also referred to the climatological phenomena in this study. Here we have rainfall immediately after washing of the car, or a cold wave as soon as the furnaces are closed down for the winter. However, Strang and Springle's extension of this law into gravitation have not been completely accepted. Their statement that things fall at right angles is completely invariant with the well known fact that toast always falls buttered side down. These are, however, only a small smattering of the applications of the law.

Finnagle's Third Law

"No matter what happens, somebody somewhere will tell you I told you so." So far no direct applications of this law have been discovered.

Finnagle's Fourth Law

"Even if it is impossible to incorrectly assemble a part, still a way will be found to do it wrong." Thus far this law has been found to be immutable.

Finnagle's Fifth Law

"Whenever a system becomes completely defined, something is discovered which either abolishes the system or expands it beyond recognition." The basis of this law has been present in folklore for countless centuries. It has provided both an optimistic outlook and a pessimistic outlook. I refer to the two sayings, "There is always room for improvement," and "No matter what you do it won't make any difference."

It is to be expected that careful study of Finnagle's laws of the universal perversity of matter will lead to the discovery of many corollaries and applications which will be useful in basic research, clinical medicine, and the enjoyment of everyday life.

These observations have been collected over many years from multiple sources — writings, word of mouth, and personal observations — so that it is not possible to give accurate credit to the original contributors. The history of the formulation of these important laws would also be a vital field for study.

Warren J. Warwick, M.D.*
Minneapolis, Minnesota

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*Assistant Professor, Department of Pediatrics, University of Minnesota.

Progress in Cervical Cytology

THE FEBRUARY issue of Minnesota Medicine* contains an article reviewing the results of a cervical cytology survey conducted by the Cancer Control Section of the Minnesota Department of Health with the co-operation of the Cancer Committee of the Minnesota State Medical Association and the Cytology Committee of the Minnesota Division, American Cancer Society. A total of 1,835 questionnaires were completed and returned by nearly half the licensed physicians in Minnesota. Of the responders, 1,684 stated that they examine the female pelvis, and 1,223 or 72.6% stated that they make routine cancer smear tests of the vaginal or cervical secretion. According to type of practice, 93.1%

Continued

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*Smith, Samuel A.: Cervical Cytology Survey, Minnesota Med 48:277, 1965.

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of the obstetricians and gynecologists, 89.8% of internists and 67.0% of general practitioners reported taking smears routinely. Over 80% of all groups preferred to take the smear test at yearly intervals, while only 64.3% advised taking the first smear test before the age of 30 years. A surprising finding was that only 34.8% of responders routinely made smear tests during pregnancy.

Many studies have shown that severe dysplasia and occasionally preinvasive or invasive carcinoma of the cervical epithelium occurs during the second and third decades of life. Young women, pregnant or not, deserve the protection of the cytology smear test as much as their older sisters. The premise that smears are inaccurate during pregnancy has been disproved. Some physicians fear that the finding of a positive smear will lead to the need for investigative procedures that may imperil present or future pregnancies. This premise too has been disproved by large series of cone biopsies performed during pregnancy with small risk of abortion. The cone should be performed after the third month of pregnancy and should be conservative in size.

A second and as yet unpublished survey was made of thirteen hospital cancer registries in the state of Minnesota during 1963 to determine the effect of the cytology smear test on the incidence of preinvasive and invasive cancer of the cervix. The data was obtained by the Cancer Control Section of the Minnesota Department of Health and was compiled by the writer. This survey which included the years 1958 through 1963 showed a sharp rise in the number of diagnoses of carcinoma in situ from 65 in 1958 to 182 in 1961. A slight decline then occurred to 173 in 1962 and 153 in 1963. During the same years the number of cases of invasive carcinoma of the cervix did not change significantly.

The failure of the Minnesota registry study to show a decrease in incidence of invasive carcinoma of the cervix is in contrast to the findings of studies in both British Columbia and Shelby County, Tennessee, where intensive population screening programs have been in process for over a decade. The British Columbia study reported a drop of 45% in the incidence of invasive carcinoma of the cervix, and the Shelby County study reported an even greater drop. In both these studies the incidence of carcinoma in situ levelled off to 46 and 45 per 100,000 women respectively. Comparison of the incidence curves of these two studies with the Minnesota registry study suggests that in Minnesota the use of cervical cytology hasn't existed long enough to show the expected decline in the number of diagnoses of invasive carcinoma of the cervix.

The ultimate value of the smear test must be judged by its ability to effect a marked drop in mortality rate for carcinoma of the cervix. The Cancer Control Officer for the Minnesota Department of Health, Dr. J. J. McCullough, obtained the following figures: for the United States a decline from 10.8 per 100,000 females in 1953 to 9.0 in 1962. In Minnesota the rates have dropped from 7.2 in 1955 to 5.4 in 1963. The decline for the whole country was 16.6% and that for Minnesota was 25%. By comparison the Shelby County death rate for white females dropped 59% from a peak of 22 per 100,00 in 1953 to 9 per 100,000 in 1961.

From the above it is apparent that Minnesota shares with other regions the great impact made on the early diagnosis of carcinoma of the cervix uteri by widespread use of cervical cytology. However, the results of these studies show little cause for complacency among those agencies charged with the responsibility for public and professional education in the area of cancer detection.

Melvin B. Sinykin, M.D.
Minneapolis, Minnesota

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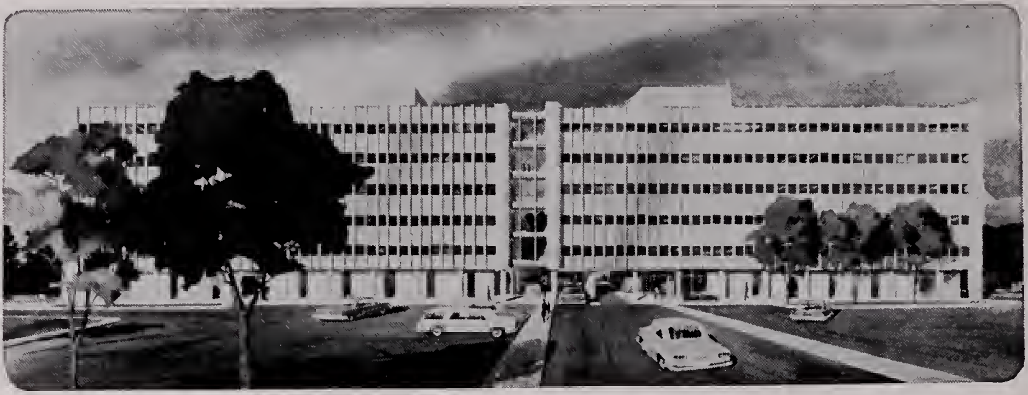

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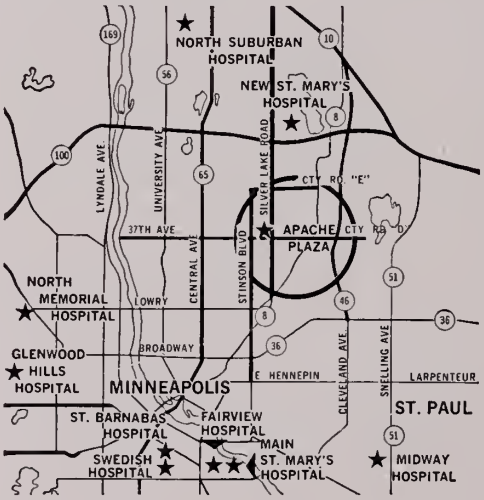
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Test Your Word Score

Retinopathy — any noninflammatory disease of the retina (page 571)
Psychotropic drug — one which acts psychologically on the central nervous system (page 573)
Estopped — law term meaning barred, prohibited (page 574)
Trichoepitheliomata — skin tumor whose cell growth starts in the follicles of the lanugo (page 575)
Dentigerous — (cyst) containing one or more fairly well-formed teeth (page 575)
Hypertelorism — abnormal width between two organs or parts (page 575)
Marsupialization — operation for hydatid by opening the tumor, emptying it and stretching the tumor to edges of external incision (page 576)
Pleurodynia — paroxysmal pain in the intercostal muscles (page 577)
Pleomorphism — assuming various forms (page 584)
Sensorium — the part of the brain concerned with reception and interpretation (page 596)
Sterism — moonface, Cushing's Syndrome (page 606)
Factitial — produced by artificial means, e.g., X-ray therapy (page 609)

The Editor's Soliloquy

A Couple of Beers

In the usual circumstance a couple is two, but in beer a couple has no numerical equivalent. It is not one and certainly not two, for the habitue whose breath discloses the indulgence would happily admit the specific one or two when apprehended, in order to absolve himself of a possible accusation of intoxication; the nonspecific "couple of beers," he opines, leaves him clear of any wrongdoing. If he is dragooned by an inquisitive officer to three or more, his memory fails him as he glibly absolves himself of any such penury as counting beers with a friend. Certainly no accusing officer would be so insular as to incriminate a man for drinking, after only a couple of beers. Not even the drunkometer would give more than a trace of alcohol from a couple of beers, but in the state of Connecticut a man* who drank "a minute amount" was found guilty of driving while intoxicated. When he was put in the cell, he pounded on the bars, tore his blanket in strips, and threatened to hang himself. He had failed the usual sobriety test. The following day he was removed to a hospital where a sympathetic psychiatrist examined him and subsequently testified that the driver's condition at the time of arrest was one of pathological intoxication, which probably could be produced by drinking a minute amount of alcohol, and that the alcohol could not be considered a causative agent but a catalyst, without which such a reaction could not occur.

The law did not distinguish between alcohol as a causative agent and as a catalyst, and the jury found that the driver was so affected by the "minute amount" of alcohol as to appreciably impair his ability to drive.

There was a strong odor of alcohol on his breath, but he admitted drinking only a couple of beers. — Carl O. Rice, M.D.

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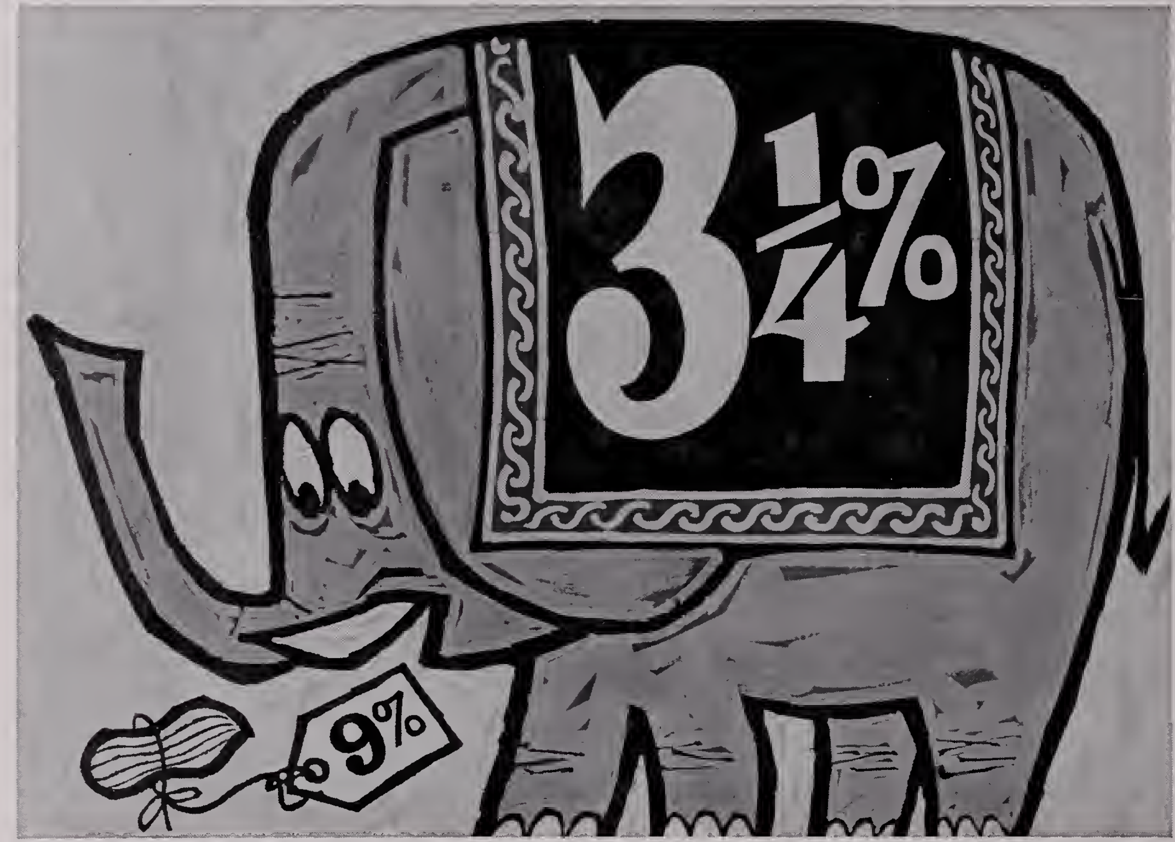
*State of Conn. vs. Holota, 194 AD 69, Conn. March '63.

Hiccough

Child's Definition: Something in my mouth makes my head shake and say "hic."
— C.McC

Riddle: When is 3¼% larger than 9%?



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MINNESOTA MEDICINE

HONOR AWARD

Minnesota Medicine Medical Writing Awards, 1965

It is the pleasure of the Board of Editors to announce the winners of the fourth annual Minnesota Medicine Medical Writing Awards chosen from articles published in MINNESOTA MEDICINE during the year of 1964.

The first place plaque is to be awarded to Dr. Robert L. Strom of the Hennepin County General Hospital; Dr. Wendell H. Hall of the Veterans Administration Hospital and Frances Casey, B.A. of Minneapolis. Their article "Coccidioidomycosis — A Minnesota Experience" appeared in the October issue of MINNESOTA MEDICINE, page 1189. The presentation will take place during the annual meeting of the Minnesota State Medical Association in Minneapolis at the New Members, County Officers and Delegates Dinner on Sunday, May 16th.

Certificates for excellence in medical writing will be awarded to the authors listed on the next page together with the titles of their articles which were felt to be particularly outstanding by the Board of Editors.

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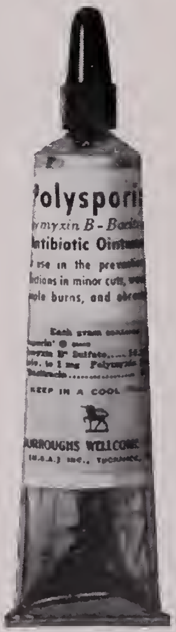

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Manuscript	*Authors*	*1964 Issue*
Extracranial Vascular Occlusive Disease — An Analysis of Fifty Cases Treated Surgically	M. F. Lynch, M.D. N. K. Jensen, M.D. W. R. Schmidt, M.D. J. J. Garamella, M.D. Minneapolis, Minnesota	March

Minnesota Medicine is honored to have this opportunity to acknowledge the work of its distinguished authors and to express to them applause, thanks and cordial best wishes.

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1. Beaser, S. B.: J.A.M.A. 187:887, 1964. 2. Marble, A.: Appl. Therap. 5:614, 1963. 3. Moss, J. M. et al.: Med. Times 92:645, 1964. 4. Linder, M. et al.: New York St. J. Med. 62:337, 1962.

Curbstone Consultation

Bronchoscopic Irrigation

QUESTION: What is the nature of the low-grade infection that requires bronchoscopic irrigation?

ANSWER: Persistent, relatively nonproductive bronchitis requires bronchoscopic irrigation. This applies particularly to the bronchitis associated with a low-grade fever under 100 degress, pressure or mild pain in the anterior chest, and slight dyspnoea or unusual tiredness on exertion, which persists for weeks or months after an acute respiratory infection has subsided. This type of bronchial congestion occurs especially, but not exclusively, in patients with some pulmonary emphysema.

J. Karl Poppe, M.D.
Portland, Oregon

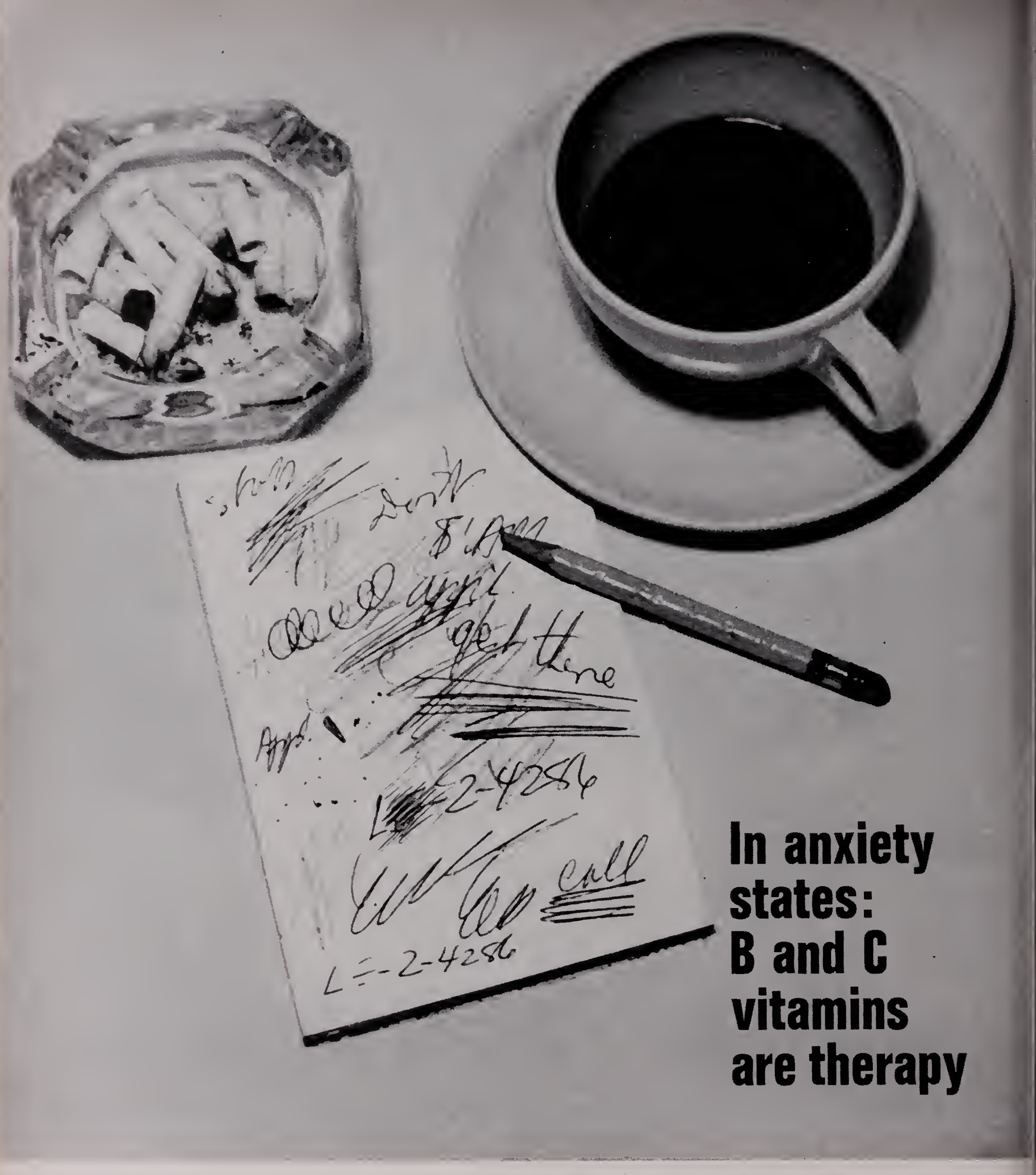
Mushroom Poisoning

QUESTION: I understand most cases of mushroom poisoning are caused by the fungi Amanita muscaria and Amanita phalloides. Is there any difference between the poisoning caused by the two species?

ANSWER: Poisoning by ingestion of Amanita muscaria is due to a parasympathomimetic agent, muscarine, with rapid onset of symptoms (minutes to two hours). Principal symptoms with this type of poisoning are lacrimation, miosis, salivation, sweating, abdominal cramps, diarrhea, vomiting, circulatory failure, coma, and convulsions. Atropine is the specific agent used to antagonize the effects of the muscarine.

Ingestion of Amanita phalloides results in poisoning created by the effects of phalloidin and other toxins in the fungus. A delayed type of intoxication (six to fifteen hours) results from these agents. In addition to the gastrointestinal symptoms, which are similar to those caused by muscarine, liver damage and renal shutdown may result. Circulatory failure and coma generally occur within about seven days. Supportive therapy particularly in the administration of protein is felt to be helpful in preventing liver damage due to phalloidin.

Medicines are nothing in themselves, if not properly used, but the very hands of the gods, if employed with reason and prudence. — Herophilus B.C. 300



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Fracture–Trauma Conference

Penetrating Abdominal Wound with Aortic Perforation

Treatment of abdominal gunshot wounds has become fairly well standardized since World War II. The principles of obligatory exploration, resection or repair of damaged small bowel, and proximal colostomy or exteriorization of damaged large bowel are well defined.[1] Early definitive treatment in civilian hospitals in peacetime, coupled with less severe injury as produced by small-bore relatively low-velocity missiles, has led some surgeons to recommend primary closure of certain of these colon defects.

One of the major advances made possible by the experience gained during the Korean War was the dictum of repair, when feasible, of important vascular structures.

The patient described in the following interesting case history recovered because of the awareness of these principles, plus rapid transfer from the scene of the accident to a major hospital facility, the 24-hour a day coverage at the hospital by a well trained resident staff, and the knowledge gained from experience with cardiovascular surgical techniques.

Case

A 30-year-old male was brought into the Hennepin County General Hospital on February 5, 1964, unresponsive and with no obtainable blood pressure. He was alleged to have shot himself in the abdomen with his own .22 caliber pistol. He was taken immediately to the emergency treatment room where a cutdown was quickly performed.

A unit of plasma was rapidly given, followed by noncrossmatched O negative blood from the blood bank. His blood pressure became detectable and rose within a few minutes to 110/60. A Foley catheter was placed in his bladder and a nasogastric tube into his stomach. His urine was clear, indicating that the bullet had probably not traversed the genitourinary tract, but the return from his nasogastric tube was bloody. The wound of entry was in the left upper quadrant and there was no wound of exit. Auscultation of his heart and lungs revealed no abnormality. A portable X ray of the abdomen revealed the bullet to be superimposed over the L2-L3 vertebral interspace.

He was taken to the operating room promptly and under a general anesthetic an exploration of his abdomen was performed. It was discovered that the bullet had passed through the stomach and that there was a large hematoma in the mesentery of the colon and small bowel. The posterior peritoneum overlying a large retroperitoneal hematoma was incised and as the clot was removed, a brisk hemorrhage ensued, coming from the abdominal aorta just proximal to the take-off of the inferior mesenteric artery. Digital pressure and Satinski clamps were used to control the hemorrhage. At this point it could be seen that the bullet had passed through the body of the pancreas, then through

Continued

the anterior and posterior wall of the abdominal aorta, lodging in the vertebral column.

The aortic perforations were closed with running 4-0 vascular silk, and after securing complete hemostasis a Penrose drain was placed down to the pancreas. The perforations in the stomach were closed and after careful examination of the large and small bowel, the abdomen was closed. The patient had been given 6500 cc. of blood.

Postoperatively there was a significant amount of pancreatic drainage through the stab wound, but this gradually subsided and he recovered to be sent to the Psychiatric Ward. He was discharged from the hospital on March 7, 1964, with no apparent residua from the bullet lodged in his spine.

Discussion

This case represents only a few of the many problems that may arise secondary to a gunshot wound of the abdomen. It is, however, particularly interesting from the standpoint of abdominal aortic perforation.

A free perforation of the lower aorta or major iliac vessels would almost certainly be lethal over the time period that elapsed from the patient's point of injury until hemostasis was achieved at surgery. In this case, however, the bullet passed through the stomach and pancreas, leaving intact the posterior peritoneum; this helped contain the hemorrhage enough so that a sufficient circulating blood volume was maintained to support life. Also, this was a small-caliber low-velocity bullet, producing two clean perforations.

It should be emphasized that if such a perforation is suspected clinically, and if the patient's vital signs give evidence of a continuing deficit in circulating blood in spite of plasma, plasma substitutes, and blood replacement, then preliminary tests should be waived and the patient taken immediately to the operating room for exploration.

Closure of the perforations with running silk sutures attenuated the diameter of the aorta to a degree. However, this seemed preferable to the placement of a patch, which we felt would be less able to withstand the effects of free pancreatic juice than would the normal aortic wall.

In gunshot wounds of the abdominal cavity, it is important to repair, remove, or drain all involved organs. Consequently the stomach perforations were closed and the pancreas drained. In this instance the postoperative pancreatic drainage did not complicate the patient's course, because an adequate cutaneous exit had been provided in advance.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

Reference

1. Surgery in World War II, Vol. II, Office of the Surgeon General, Department of the Army, Washington D. C. 1955.

The physics of a man's circulation are the physics of the waterworks of the town in which he lives, but once out of gear, you cannot apply the same rules for the repair of the one as of the other. — William Osler

---

Few people who make "footprints in the sands of time" are wearing loafers.
— The Pana (Ill.) News-Palladium

He's the best physician that knows the worthlessness of most medicines.
— Benjamin Franklin

Tumor Conference

Common Duct Tumor Mimicking Stone

Cholangiography, preoperative, operative, and postoperative, is an invaluable adjunct to the study and treatment of biliary tract disease. A high degree of accuracy in the interpretation of these roentgenograms has been achieved.[1] But it must be emphasized that errors in interpretation do occur, and clinical judgement and repeated, careful re-examination are often necessary in arriving at a diagnosis.[1,2]

Cholangiograms may fail to show stones or tumors when too dense a contrast media is used to fill large duct systems, or when poor films are accepted for interpretation. Air bubbles or spasm of the sphincter may simulate stones or tumor. Enlarged lymph nodes may produce apparent intraluminal defects indistinguishable from stones.[3]

An unusual problem of differential diagnosis of stone and tumors is illustrated in this case.

Case History

A 44-year-old man was admitted to the hospital on May 2, 1961, complaining of severe headaches, nervousness, and tremor of the hands. He also said that for the past five or six months he had had occasional abdominal cramps that would come on after meals, last for five or ten minutes, and then be relieved by drinking carbonated beverages. These cramps were occasionally severe enough to cause him to break out in a cold sweat. The pain radiated over the entire abdomen. Onions, cucumbers, radishes, and occasionally coffee would initiate an attack. Fatty foods did not cause any particular difficulty.

He had been operated on for appendicitis in 1950 and for an inguinal hernia in 1956. Six or eight weeks prior to admission he noticed that his stools resembled tar for a period of several days.

Physical and Laboratory Findings

The physical examination was noncontributory, except that on abdominal examination a slightly tender mass could be palpated in the right upper quadrant. The rest of the abdominal examination was normal. Routine blood, urine, and serological examinations were also normal. One-minute bilirubin was reported as 0.10 mg. and total bilirubin 0.70 mg. per 100 cc. of serum.

His chest film was also reported as normal. X-ray examinations of the abdomen showed a large shadow in the right quadrant resembling a hydrops of the gallbladder. No gallbladder shadow could be seen on the cholecystogram. Studies of the upper and lower gastrointestinal tract and the urinary tract were normal

Continued

Operative Findings

He was brought to surgery and a hugely distended gallbladder found and removed. The common duct was dilated and opened; three small fragments of stone were found and removed. A 4-millimeter probe was passed through the sphincter of Oddi into the duodenum, a T-tube was inserted, and a cholangiogram was done. No defects were seen on the films; and though no dye was seen in the duodenum, the duct was considered patent, and the abdomen was closed.

The pathologist reported that the gallbladder was ulcerated and dilated, with a hemorrhagic infiltration of the wall. The largest stone measured two millimeters in diameter.

Progress

The patient had an uneventful postoperative course. A T-tube cholangiogram was done one week after surgery. The common duct was dilated, and there was a definite narrowing of the distal portion of the duct, which the radiologist thought might be due to a nonopaque stone or a stricture. Dye entered the duodenum readily.

It was possible to clamp the T-tube without causing the patient any distress. He was discharged from the hospital twelve days after surgery and followed with monthly cholangiograms, which consistently showed a dilated common duct proximal to a "ring-like" defect in the distal portion of the duct. It was the impression of several radiologists that the findings were those of gallstone obstruction of the distal common duct.

Six months later he was admitted to St. Barnabas Hospital for choledochotomy. On the preoperative T-tube cholangiogram a ringlike defect was seen in the distal portion of the common duct. Because it appeared that the dye completely encircled the defect (Figure No. 1), the defect was thought to be a radiolucent stone.

The man was again brought to surgery and the abdomen opened through the previous subcostal incision. After freeing the adhesions the duodenum was mobilized, but no stone could be palpated. The T-tube tract was cut off flush with the common duct and readily passed through the ampulla

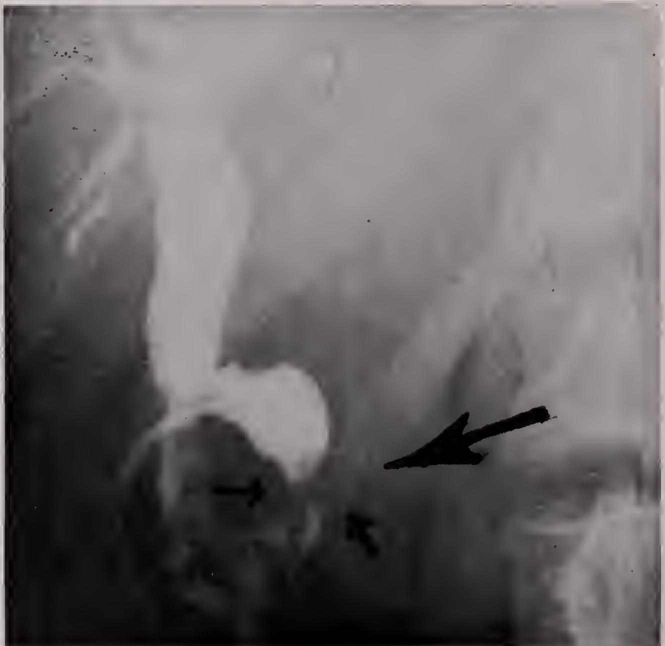

Fig. 1

of Vater into the duodenum. Stone forceps and scoops were passed down to the ampulla, but no grating or sensation of stone was noted. A number 6 dilator was then passed down the duct. This stopped at the point of maximal narrowing. Stick-ties were placed in the duct and the duct was opened at this point. It was then possible to identify a firm, round lesion measuring 10 millimeters in diameter attached to the medial wall. The lesion was excised with the terminal portion of the common duct and submitted for frozen section.

The pathologist reported that the common duct contained a poorly differentiated adenocarcinoma apparently arising from the glands of the common duct.

It was then decided to do a "Whipple procedure." Approximately one-third of the stomach was resected. The jejunum was sectioned distal to the ligament of Treitz. The common duct was transected proximal to the area where the T-tube had been placed. The pancreas was transected to the left of the portal vein.

Because the pancreatic duct was very small, the neck of the pancreas was inverted into the open end of the jejunum and sutured in place. The common bile duct was anastomosed to the jejunum two inches distal to the pancreatic anastomosis. The stomach was anastomosed to the side of the jejunum approximately eight inches from the choledochojejunostomy.

The patient tolerated the procedure well. When last seen on October 9, 1964, he was working full time, had maintained his weight at the postoperative level, and there were no evidences of recurrence.

Comments

"Classical signs" are not infallible. Repeated examination and attention to clinical findings are important. In this case perhaps the dilated biliary ductile system and gallbladder indicated the need for a better "cause" than "three small stone fragments." The diagnosis of carcinoma of the common bile duct prior to the onset of clinical jaundice is so uncommon that this diagnostic possibility is easily overlooked. The lack of growth of the lesion over a period of six months is striking. Some of the larger lesions involving most of the circumference of the duct must be present many months before jaundice occurs.

E. Theodore Palm, M.D.
Lyle J. Hay, M.D.
Minneapolis, Minnesota

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M.M.

Neuro-Pediatrics Conference

Tuberous Sclerosis*

(Bourneville's Disease)**

This six-year-old white male was referred to the University of Minnesota Hospitals in November, 1963. He was the product of a normal pregnancy and a 48-hour labor. There was a prolonged second stage of delivery, and forceps were required. Examination of the newborn showed a cephalohematoma in the left occipitoparietal region and a mark on the face from the forceps. During the neonatal period he was fussy and irritable, had difficulty in handling his secretion, coughed and choked frequently. His developmental milestones were reached at the appropriate times. At 22 months of age he had a Coxsackie pharyngitis and a concurrent generalized convulsion characterized by stiffening and clonic movements of all extremities. A second generalized convulsion occurred later the same day. At age two he had a convulsion which lasted a little over an hour, associated with high fever, and at this time, he was hospitalized. An electroencephalogram was questionably abnormal, and he was discharged on phenobarbital. From age two to age 3½ he had short major convulsions every three months. In the spring of 1961 he began to have brief seizures characterized by lapse of consciousness and tightening of the muscles around the mouth. Dilantin® was added to the phenobarbital in an attempt to control these seizures, but he began to have more lapses, with his eyes rolling up and momentary cessation of all motor activity. He was then started on Tridione® and Mebaral.® In the fall of 1961, he was taking phenobarbital, Tridione,® and Dilantin.® His behavior became very difficult to manage and Thorazine® was added to his therapeutic regime. He continues to have generalized seizures once every three months, but had none in the year before coming to the University Hospitals. In the fall of 1963, his comportment became progressively worse, with agitated, hyperactive and erratic behavior. The past history and the review of symptoms are otherwise noncontributory. The family history shows no evidence of neurological disease. The patient's mother is a kindergarten teacher and appears very understanding of the entire situation.

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*Held on Wednesday, November 18, 1964, at 3 p.m.

Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatric conferences are held the first and third Wednesdays of every month from 3:15 to 4:15 p.m. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Robert W. ten Bensel, in Pediatrics, and Dr. Robert Soll, in Adult Neurology.

**See Minnesota Med 47:271, 1964.

Continued

Dr. James DeVinck*

He appeared to be a well-developed, well-nourished, six-year-old male, who showed extreme hyperactivity during the entire examination. There is evidence of marked fluctuation in his attention span. His head circumference is 52 cm. Over the nose and cheeks there are very minute papular lesions measuring 1 to 2 mm. in diameter. There are several areas of vitiligo over the backs of the legs.

The remaining examination was normal except for mild bilateral incoordination of cerebellar nature. X rays of the skull were normal, showing no calcification. An electroencephalogram was reported as moderate to markedly abnormal with frequent multifocal isolated spike activity, mainly on the left. There was bilateral synchronous isolated spike and wave activity of high amplitude on the left, appearing to come from a deep focus. Because of the diagnosis of tuberous sclerosis, a consultation with dermatologists was obtained, their impression being that the skin lesions over the face were classic of adenoma sebaceum and that a biopsy was not necessary.

At this time, the child was started on phenobarbital, 60 mgm. three times a day and Desoxyn,® 5 mg. twice a day. After two weeks his hyperactivity diminished and his general behavior pattern improved. He still continues to have several seizures a day, but they appear less severe.

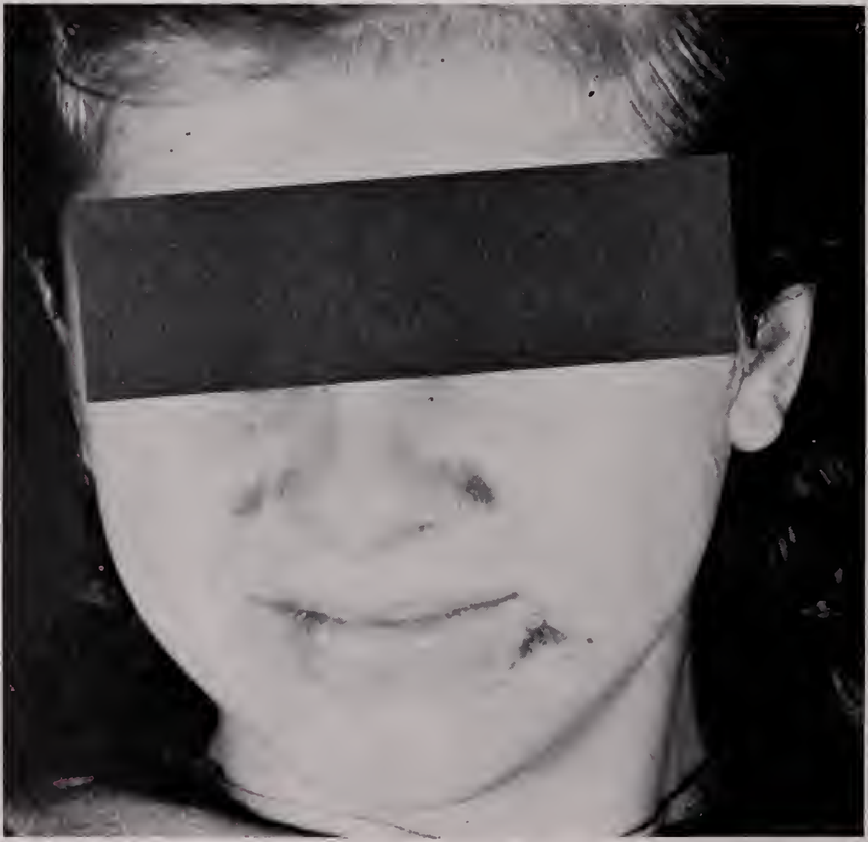

Fig. 1 — Adenoma sebaceum in a patient with tuberous sclerosis. Lesions may be very mild in young children but may be very prominent in the adult. (Fig. 2)

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*Student physician, University of Minnesota Medical School.

Presently the phenobarbital dosage is 60 mg. in the morning, 60 mg. at 2 p.m., and 90 mg. at bedtime. He was tried on both Zarontin® and Celontin,® but again his behavior became worse, showing more irritability, destructiveness and inco-ordination.

In March of 1964 there was marked improvement in his behavior and he became more manageable; also his report card became more satisfactory. He was last seen October 28, 1964, at which time his seizures were essentially unchanged except that a few had been noted at school. The seizures occur in the morning with flexion of the head and chin. His behavior is generally good, but occasionally he had a poor day in school. At his last clinic visit he was begun on Librium,® 5 mg. twice a day.

Mrs. Ruth Agar*

At the present time he is reading a primer of 135 words and seems to have a good vocabulary with slight to good comprehension. Occasionally he blocks on words and in his ability to concentrate. He can write one to seven numbers, but it is felt that his understanding of the symbols is not clear. At times he needs to repeat his work and begins to stammer when he is excited. He appears to enjoy books and retells the stories which he hears. When working alone, he is easily distracted and, at times, "silly." He is in need of constant adult supervision in play and work.

Mrs. Hemstock**

He has petit-mal seizures every morning before attending school. His

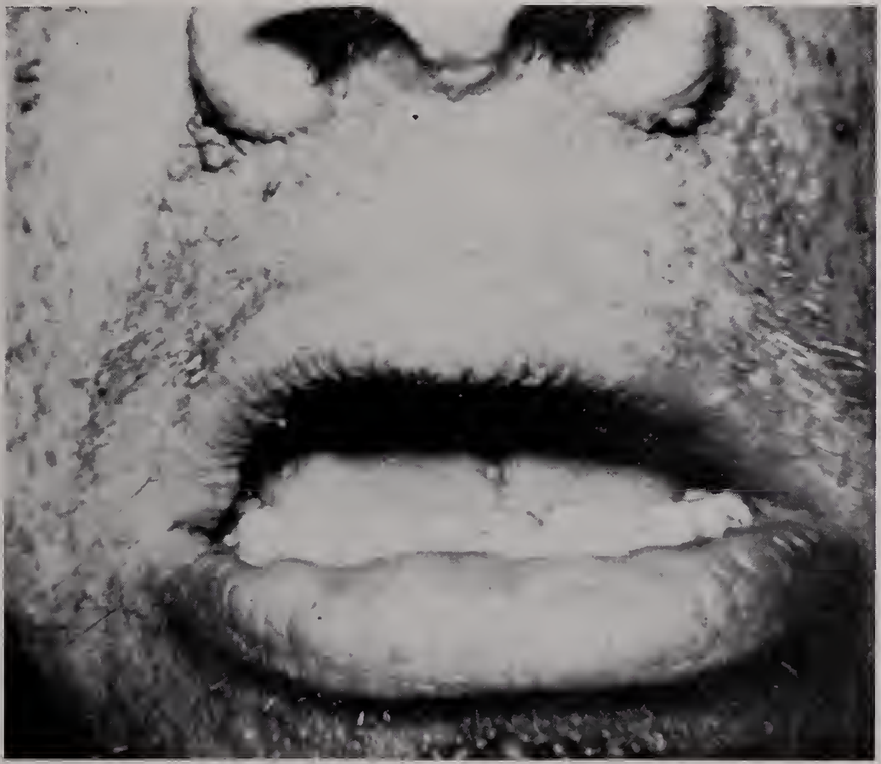

Fig. 2 — Adenoma sebaceum in an adult associated with tuberous sclerosis.

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*School social worker, Robbinsdale, Minnesota.
**School nurse, Robbinsdale, Minnesota.

Continued

mother does not usually dress him until after his seizures, as he urinates at this time. Two weeks ago, when his medications were changed, he suddenly became very accident-prone as a result of increased inco-ordination. The communication between the mother, school nurse, and school teachers is very good regarding his changes in medications. His school health record contains most of the pertinent information which is communicated from the mother to the school nurse.

Dr. Kenneth Swaiman*

Tuberous sclerosis is an uncommon neurological condition. This syndrome clinically consists of adenoma sebaceum, seizures, and difficulty with learning (mental deficiency). The course is progressive, as it appears to be in this patient. The findings which the patient manifests would assure one of the diagnosis of tuberous sclerosis with 95 to 98 per cent accuracy. The skin lesions are very striking when they are present, characterized by a nose blush of a papular, discrete character. They are caused by an increase of connective tissue and an increased capillary venular pattern, as well as associated increase in sebaceous glands. In the central nervous system the classical lesions are convolutional foci of sclerosis in which the gliosis is associated with gross disturbances of architecture.[1] These areas of gliosis may enlarge, forming "tubers" over the cortex, in the white matter and in the subependymal areas of the ventricles. In time these tubers may become malignant and grow very rapidly, similar to the glioblastoma multiforme of the adult. Brain tumors, however, are rare; among 29 patients Critchley and Earl[2] found only one example. The disease is not confined strictly to the central nervous system, as there may be an involvement of the heart, bones and kidneys. In the heart the disease is usually associated with rhabdomyomas, while the kidneys and bones may have hamartomas. The skin may also show discoloration over the area of the lumbar spine, called "shagreen" spots. Various developmental defects

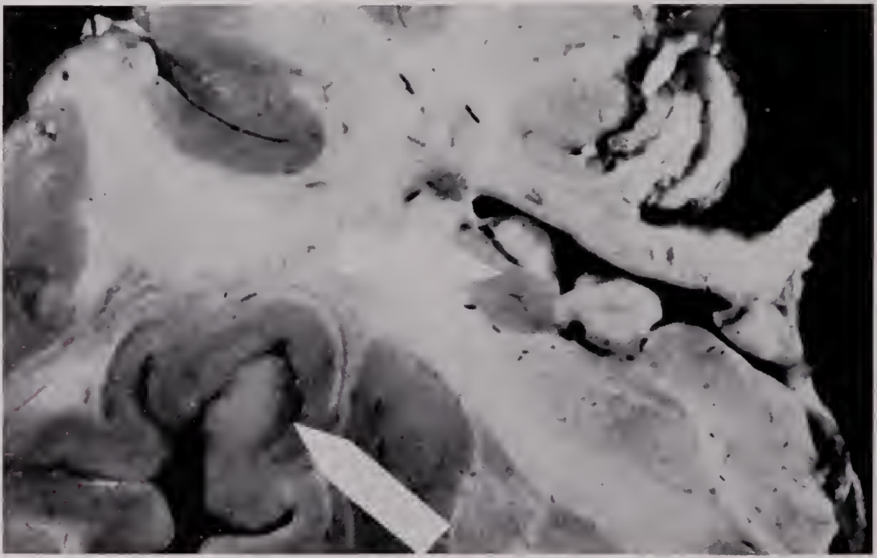

Fig. 3 — Subependymal and cortical tubers in tuberous sclerosis. Subependymal tuber is protruding into the lateral ventricle. (Coronal section of brain.)

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*Pediatric neurologist, University of Minnesota Medical Center.

may also be found, such as congenital heart disease, harelip, spina bifida, and polydactylism.[3] The lungs are rarely affected.

The prognosis for this child is poor. Both his intellectual life and his social life are already compromised. Nothing is known that has been beneficial so far in halting the progressive nature of the disease and death often occurs early in the second decade.[3]

Dr. Edward Defoe, Jr.*

Tuberous sclerosis is usually considered a dominant disease with incomplete penetrance, although it may be sporadic in nature. This case probably represents a sporadic case, as there is no family history of the disease.

Dr. Harold Ireton**

In April 1964, the patient attained a score of 62 on the Stanford-Binet. His ability to identify pictured objects by name was less than adequate for an average four-year-old child. His ability to state the meaning of words was slightly better, but none the less below average for a child of his age. He should have yearly psychometric testing to determine whether there is any progression in his mental retardation. The parents might benefit from supportive counseling.

Mrs. Helen Moon†

The parents do need encouragement about the child's progress in school. In the Robbinsdale school system there are classes for those children with I.Q.'s of less than 80. The classes for the neurologically damaged are for those children with I.Q.'s above 80 and who have neurological handicaps. There are also eight rooms for slow learners.

Final Recommendations of the Conference

1. Dr. Roger Lienke‡ will work closely with the University staff in maintaining communication with the school as far as changes in medication and any further progressive neurological changes are concerned.
2. It is recommended that psychological testing be performed at fairly frequent intervals of one to two years to evaluate any further progressive mental retardation.
3. Those persons involved with the patient on a day-to-day basis should seek to give the parents emotional support in the handling of their child.

Robert ten Bensel, M.D.
University of Minnesota Medical Center

Those Participating in the Conference: Dr. Roger Lienke, Referring Physician; Mrs. Hemstock, School Nurse, Robbinsdale School System; Mrs. Ruth Agar, School Social Worker, Robbinsdale, Minnesota; Mrs. Helen Moon, Special Education Teacher, Robbinsdale, Minnesota; Dr. James DeVinck, Senior Medical Student; Dr. Kenneth Swaiman, Pediatric Neurologist; Dr. Harold Ireton, Clinical Psychologist; Dr. Robert ten Bensel, Moderator.

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*Director, Pediatric Clinic; associate director Comprehensive Clinic, University of Minnesota Medical Center.

**Clinical psychologist, University of Minnesota Medical Center.

†Special education teacher, Robbinsdale School System.

‡Referring physician, Robbinsdale, Minnesota.

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Advances

Infections of the Urinary Tract

Part V — Comments and Conclusions*

WILLIAM J. MARTIN, M.D.**
RICHARD D. WAGONER, M.D.**
Rochester, Minnesota

Toxic agents that may accumulate in the blood, such as streptomycin and even the bacteriostatic sulfonamides, nitrofurantoin, nalidixic acid, and methenamine mandelate, should be used with caution in patients who have borderline renal insufficiency. If renal function is less than normal, the doses of such drugs should be correspondingly reduced or eliminated.

There are four antibiotics capable of ototoxicity: streptomycin, neomycin, kanamycin, and vancomycin; by allowing these agents to accumulate in the blood, renal insufficiency may increase their ill effects on the eighth cranial nerve. Detection of early vestibular and cochlear complications can best be effected when audiometric and vestibular turning tests are done before therapy with a potentially ototoxic antibiotic is begun, periodically during treatment, and again six months after its cessation. Concurrent use of ototoxic drugs should be avoided and caution should be exercised in patients to whom such drugs have been administered previously. Older patients especially should be carefully observed for signs of damage to the eighth cranial nerve.

Agents described as having a potentially direct nephrotoxic effect are the sulfonamides, streptomycin, neomycin, kanamycin, bacitracin, vancomycin, polymyxin B, colistin, amphotericin B, and outmoded or degraded tetracyclines. Whether methicillin and cephalothin have such an effect is uncertain.

Penicillin, erythromycin, and chloramphenicol are three antibiotics of which the renal route of excretion is largely tubular; consequently in azotemic patients receiving these drugs, there is less concern regarding abnormally high blood levels and their duration than with drugs having a glomerular route of excretion.

Antibiotics capable of producing neuromuscular block similar to that induced by d-tubocurarine chloride include streptomycin, dihydrostreptomycin, neomycin, kanamycin, and polymyxin B. Colistin may have a similar effect. Curare-like effects have been noted after instillation of these drugs intrapleurally as well as intraperitoneally. Similar effects have followed intravenous administration of kanamycin, which might alert one to the possibility of their appearance when polymyxin B is given by that route. Anoxia, sometimes associated with anesthesia, may enhance the antibiotic-induced curare-like effects. Failure to reverse the untoward reaction may eventuate in respiratory and cardiac arrest. Neostigmine and calcium gluconate have been suggested in management of the reaction. The physician should bear in mind the theoretic possibility of this effect in patients receiving neomycin-polymyxin B rinse via indwelling urethral catheter.

Administration of a sulfonamide in full dosage to a woman near term requires caution because of the possibility of producing hyperbilirubinemia by releasing protein-bound blood bilirubin with consequent kernicterus in the fetus. Probably all sulfonamides are contraindicated for premature and newborn infants for the first weeks of life because of their undeveloped enzyme systems and immature hepatic and renal function.

Nephrotoxicity due to the sulfonamides may occur via two mechanisms: (1) precipitation of the drug, especially the acetylated derivative, in the tubules, and (2) hypersensitivity. Crystallization in the renal tubules is encouraged by a less than adequate

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*See Part I, Minnesota Med., January issue, Page 95, Part II, February issue, Page 231, Part III, March issue, Page 379 and Part IV, April issue, Page 503.

**Section of Medicine, Mayo Clinic and Mayo Foundation.

daily output of urine. Because the solubility of both free and acetylated sulfonamide is greater in a neutral or alkaline medium, alkalinization of the urine has been attempted in an effort to decrease crystallization. However, alkalinization increases the rate of excretion of the sulfonamide, lowers the concentration in the blood, and requires increased administration to produce tissue bacteriostasis. Sulfisoxazole (Gantrasin) and sulfisomidine (Elkosin) are more soluble in urine of variable pH than are sulfadiazine and sulfamerazine. Special care may be required with sulfamethoxazole (Gantinol) to avoid crystalluria because of the high degree of acetylation of the drug in the urine.

In certain infections in which response is incomplete and in which microbiologic studies demonstrate that the pathogen remains sensitive to an antibacterial regimen, continuation of the same regimen, perhaps with increased dosage, may control the process. In other words, failure of response may reflect either the duration or the total dosage of the regimen employed and does not necessarily require resort to a different drug.

Adjustment of urinary pH has been said to enhance the activity of drugs in the management of urinary infections.[21] Antibacterial activity of streptomycin, neomycin, kanamycin, penicillin, and erythromycin against organisms causing urinary infections may be augmented at alkaline pH, whereas the tetracyclines, cycloserine, and novobiocin may be more potent at acid pH. It is said that results with sulfonamides and chloramphenicol vary with the organisms tested, and that the action of nitrofurantoin is not influenced by pH adjustments. A 20 per cent increase in effectiveness has been claimed for the procedure.[21]

Cycloserine (Seromycin) may have a place as a second-line agent in the management of selected infections of the urinary tract when conventional agents have failed and before drugs with greater toxic potential are employed. In addition to its tuberculostatic effect, cycloserine is active against coli-aerogenes and enterococcal and staphylococcal organisms; Pseudomonas and Proteus organisms often are resistant to the action of the drug. In-vitro susceptibility testing should be carried out with a synthetic alanine-free culture medium because of the phenomenon of alanine-cycloserine antagonism. In adults with normal renal function, the maximal oral dosage is 250 mg. of the agent every six to 12 hours, and blood concentrations of cycloserine in the range of 25 to 30 μg. per milliliter should not be exceeded. Side effects are most likely to occur after administration of more than 1 gm. of cycloserine daily, particularly when the individual dose exceeds 250 mg. Reportedly, untoward effects of cycloserine on the nervous system, such as mental confusion, hypomania, dyskinesia, and convulsions, are controlled by administration of pyridoxine alone or in combination with anticonvulsants. The drug should be used cautiously in face of renal dysfunction and is contraindicated in epileptics.[20]

Combinations of antibacterial agents should be reserved for situations demanding coverage while microbiologic data are awaited, for polymicrobic infections, and for instances of infections in which there are indications that an enhanced effect is possible. The use of multiple agents not only is unnecessary in most cases of urinary infection but might increase bacterial resistance more than if patients were treated with a minimal number of antibacterial drugs. Indiscriminate use of multiple agents may increase bacterial resistance, since such resistance appears to be a direct function of the total amount of a given antibacterial drug used in a given community.

It should be constantly recalled that antibacterial agents are not an unmixed blessing, because their use may result in a diagnostic loss if they are employed before diagnosis is established; they may cause emergence of resistant organisms; they may produce untoward reactions, and they are expensive.

Patients with acute pyelonephritis frequently are rather ill and should be at complete rest in bed. They may require hospitalization and intravenous fluids to combat dehydration. If there is no contraindication, fluids should be forced until the daily intake exceeds 3000 ml. Acute infections of the urinary tract should be treated for at least one week after all symptoms have subsided and after the results of cultures are negative; chronic infections warrant even longer treatment after arrest of the process. It is important that prior to cessation of therapy, additional urinalyses and cultures be obtained, and these should be repeated one to three months after treatment is stopped, or sooner if symptoms warrant. The optimal duration of treatment in an individual urinary infection actually is not known, and it may be that conclusions in this regard cannot be generic. However, it appears that as one's experience with antibacterial agents has increased in the management of urinary infections, the recommended duration of treatment has correspondingly lengthened. Treatment of acute infection of the urinary tract usually is much more successful than is treatment of chronic infection. In most cases, vigorous therapy with a pertinent drug controls acute infection if obstruction is not present. However, chronic infection is often compatible with many years of life. Even when decompensation appears, it may progress so slowly that the individual maintains his usual activity for months or years despite considerable azotemia. "Cure" can be determined only by the patient's response from both the clinical and the laboratory point of view after cessation of therapy.

In patients with persistent or recurrent infection that prompts more complete investigation, a minimal study should include determination of the blood urea, repetition of urinalysis and urine culture with in-vitro susceptibility studies, intravenous pyelography, cystoscopy, and, if possible, a cinefluoroscopic study.

In addition to the relieving of any obstruction to the passage of urine before antibacterial agents can become effective, surgical procedures such as drainage of an abscess or nephrectomy occasionally are necessary. Adequate removal of demonstrated obstruction may bring about cure of an infection, but more often eradication of pathogens in such cases requires conjoint antimicrobial therapy. Pyelonephritis is at least 10 times more frequently found in an obstructed urinary tract than in a normal one.

Infection may persist in spite of therapy, especially when bacteriostatic agents have been used. Scrutiny should not be relaxed because urine cultures become negative, especially after the use of bacteriostatic agents; later events may indicate that the infection was not completely controlled but continued to smoulder despite the negative cultural results, and it becomes acutely manifest after a short time. This is why, in more than simple acute infections, an antibacterial regimen with a bactericidal effect often is preferred, considering comparative toxicity and routes of administration. Eradication of bacteriuria during or shortly after the cessation of therapy indicates only achievement of an adequate antibacterial effect in the urine but does not assess the value of the regimen in deep-seated infections. Some of these infections "burn out"; some may continue indefinitely without appreciable deterioration of renal function, and some may culminate in renal insufficiency.

Failure in the management of an infection of the urinary tract should prompt consideration of the nature of the lesion, since underlying disease may make recovery impossible.

Conclusions

The principles of management in infections of the urinary tract can be summarized as follows: (1) identify bacteria by the gram stain and procure cultures and bacterial susceptibility tests in more severe, recurrent or chronic infections; (2) when bacteria are identified, initiate treatment with antibacterial agents on an empirical basis if the condition of the patient warrants; (3) search out and attempt to correct any condition that predisposes to infection; (4) initiate procedures to assure free access of the antibacterial agents to the site of the infection, and (5) ensure adequate drainage of the urine when indicated. Since acute, simple infections of the urinary tract are common, use of nonantibiotic antibacterial agents such as the sulfonamides in the

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therapy of urinary infections has a continued place in the therapeutic armamentarium; however, diagnosis should be as exact as possible so that treatment of more serious infections with less than adequate agents is avoided. If agents such as the sulfonamides fail to eradicate an infection that appeared to be an acute simple one, then further urologic and microbiologic investigation should be carried out.

An outline of the antibacterial regimens currently applicable to urinary infections might be the following:

1. Preliminary empiric therapy, often in the form of nonantibiotic agents, is given patients with acute infection but without overt evidences of underlying uropathy or predisposing disease. 2. Definitive therapy is given patients with infections that remain after attempted correction of uropathy, patients with marked systemic reaction especially if prior therapy has been unsuccessful, or patients in whom a last desperate effort is being made to preserve renal function. (In these and similar patients, antibiotics are generally used and then in accordance with careful microbiologic and urologic investigation.) 3. Intermittent prophylactic therapy is one in which chemotherapy is given the first five to seven days monthly for several months to patients with acute recurrent infection after negative investigation for underlying uropathy or predisposing disease. 4. Suppressive therapy is given patients with chronic infection not susceptible to eradication but in whom attempts to minimize renal damage and symptoms are made. Often nonantibiotic agents, except possibly nitrofurantoin, are used and may be given continuously or intermittently, or drugs may be alternated in an attempt to avoid unilateral dislocation of the body flora and induction of bacterial resistance. Use of nitrofurantoin is avoided in some of these patients since long-term therapy in patients with decreased renal function may be complicated by polyneuropathy. Although permanent sterilization of the urine in chronic, complicated infection may be achievable in no more than 20 per cent of cases, infection can be eliminated temporarily in about 70 per cent. With this latter rate of achievability in mind, suppressive therapy is desirable in an attempt to minimize renal destruction.

Asymptomatic bacteriuria may be demonstrated prior to the onset of clinical manifestation in acute and recurrent infections. Under such circumstances the nonantibiotic antibacterial agents are often used just as they are employed in more overt infections. As an example of such management, administration of a sulfonamide to a pregnant woman may eliminate the bacteriuria and prevent acute pyelonephritis. When asymptomatic bacteriuria manifests chronic infection and when obstructive uropathy and predisposing disease are eliminated, definitive therapy may be attempted. If such treatment is not pertinent or has been unsuccessful, suppressive therapy can be given. Asymptomatic bacteriuria is most often detected because of close scrutiny given to likely victims.

Careful analysis of the individual infection and the use of common sense in therapy are urged; there is no place for diagnostic or therapeutic dogma in urinary infections. Not all urinary infections can be eradicated any more than can all disease in any sphere of medical endeavor, but failure to control a given urinary infection promptly should not generate pessimism sufficient to cause abandonment of all therapeutic effort. It may be necessary at any stage in the management of infections of the urinary tract to re-evaluate, re-examine, and alter any regimen. Adequate management of infections of the urinary tract requires close cooperation between the internist and the urologist in selected cases. Careful follow-up of every patient having had infection of the urinary tract is mandatory.

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Grand Rounds

Polycystic Kidney Disease*

In spite of the extensive medical literature that has accumulated about polycystic kidney disease, its etiology and treatment are still not well understood, and the disease has a poor prognosis.

Etiology

In the course of the last century, a number of theories were proposed but none accepted universally.

Virchow in 1856 reported that the cysts were formed secondary to obstruction of the urinary flow, caused by uric-acid crystals or atresia of papillary ducts secondary to pyelonephritis or papillitis.[1]

In 1856 Kupffer showed that the kidney was formed from two different sources: the mesonephric duct and the metanephrogenic anlage. Hildebrand in 1894 postulated that the etiology of polycystic kidney was due to the failure of these two parts to unite.[2] Albrecht, Herxheimer and Nicholson proposed that the etiology was neoplastic.[2] Kampmeir in 1923, and also with McKenna in 1933, proposed that there was persistence of the first, second and third generation "nephron." Those "nephrons" usually disappear, but in polycystic kidney disease they may persist and subsequently lead to cyst formation.[2]

Heplers in 1930 suggested that reduction in the renal blood flow leads to cystic degeneration of the kidney.[3] Roos in 1941 attributed the etiology to defective germ plasm.[2] Lambert in 1947 showed with serial kidney sections that many adult cysts communicate with tubules, while in the neonatal polycystic kidney the cysts are closed.[4]

Bricker and Patton in 1955 demonstrated with inulin and P-aminohippurate injection that many of the cysts in adults, but only a few of those in children, were in functional connection with open nephrons. These facts, together with the finding of hereditary polycystic kidney in goldfish which

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*Medical Grand Rounds, Mt. Sinai Hospital, December 22, 1964.

have a mesonephric kidney, tend to rule out the earlier theories of Hildebrand and Kampmeir.[5]

Allen postulated that the normal development of the ureteric bud has an "organizer" effect on the metanephrogenic mass which permits canalization of tubules. Defective action of this "organizer" may result in atresia of tubules and subsequent cyst formation.[6]

Recently Potter and Osathanondh, by applying microdissection technique on kidneys from 70 normal foetuses, infants, and adults, demonstrated that the collecting tubules develop from repeated branching of the ureteral bud. The first branches of ureteral bud consist of the ampullary portion, which is the area of growth at the end of the tubule, and the interstitial portion. The ampullae normally induce formation of nephrons, then disappear; while the interstitial portion of the tubule persists.[2] In comparison, they did microdissection on cystic kidneys obtained from 30 patients with polycystic kidney disease, ranging in age from newborn to 67 years and found that the main abnormality was in the collecting tubules. They described four pathogenetic types of polycystic kidney:

Type 1: Bilateral symmetrical enlargement of the kidneys where the surfaces are essentially smooth, although they contain small cysts, 1-2 mm. in diameter, due to hyperplasia of the interstitial portions of the collecting tubules. This condition is always accompanied by intrahepatic cystic proliferation of bile ducts and, to a lesser extent, by cysts in the lungs or pancreas, and is invariably fatal in early life. This is the only variety found in siblings and may be caused by a homozygous state of recessive genes.

Type 2: Either bilateral, unilateral or only part of one kidney affected. When both kidneys are involved, the condition is always fatal after birth. When unilateral or when only part of the kidney is involved, the condition may be found in childhood or adulthood; or it may be symptomless. This variety is associated with malformation of other organs but not accompanied by hyperplasia of bile ducts. The main abnormality in this type is inhibition of ampullary activity, resulting in cessation of nephron formation, prevention of the tubules from further branching, and subsequent cyst formation.

Type 3: Always present at birth and usually bilateral, with the kidneys larger than normal. Frequently a family history of polycystic kidney is found. The abnormalities are in both the ampullary and interstitial portion of the collecting tubules. The most common sites of cyst formation are the angle of Henle's loop, Bowman's capsule, and the proximal convoluted tubules; all the cysts are connected to the tubules which communicate with the renal pelvis. The age at which the symptoms become manifest varies according to the proportion of normal to abnormal tissue. In general, this group includes all bilateral cystic kidneys found in individuals more than a few weeks of age. This type is generally designated as polycystic kidney of adults.

Type 4: Caused by urethral or ureteral obstruction in early foetal life, resulting in back pressure which subsequently affects the tubular development, resulting in cyst formation. The severity of the disease depends on the degree and the time of onset of obstruction.

Incidence

Bell in 1950 examined combined statistics of autopsy material collected from the literature and found an incidence of 1:351.[1] He also found that in 240 stillbirths the incidence increased to 1:200. Campbell studied 19,046 autopsies in children and found 72 cases, i.e., an incidence of 1:265, with a slightly higher incidence in males.[3]

Book in 1951 found in a Swedish group an incidence of 0.7 per 10,000 births.[1] Simon and Thompson studied 366 cases of polycystic kidney seen at the Mayo Clinic in the period between 1925 and 1944 and found a clinical incidence of 1:2438 and an autopsy incidence of 1:323. In the same series, 80% of the patients were in the fourth to sixth decade. The average age was 44 years; 55.5% were males and 44.5% females.[7] Most authorities agree that there is no sex predilection, and in many instances the disease is transmitted by a recessive autosomal gene which appears at two age peaks, in infancy and in adulthood, and is frequently associated with other anomalies.

Pathology

Gross

Rall and Odell in their review of the literature found that the disease affects one kidney in 4 to 13% of cases.[8] Campbell considers the incidence of unilateral polycystic kidney not to be reliable since the opposite kidney, which appears grossly normal, may be involved microscopically.[3] Macroscopically the kidneys are usually enlarged and the surface is irregular and knobby due to the presence of cysts which vary in size from microscopic to several centimeters in diameter. In infants the cysts are mainly small, so that the surface may be finely pored.[1]

The cut surface has a honeycomb appearance. The cysts contain fluid which may be thin watery, yellowish or dark brown due to hemorrhage or frank pus from secondary infection.[1] According to Campbell, the cystic fluid has a specific gravity of 1.004-1.006 and may contain cholesterol, leucine, cystine, uric acid, calcium, oxalate, red blood cells, or pus cells.[3]

Microscopic

The cysts are distributed in cortex and medulla. They are lined by cuboidal epithelium which is usually flattened, and there is infiltration of macrophages, red blood cells, and white cells.

Associated Diseases

According to Simon and Thompson there is associated nephrolithiasis in 14.1% of the cases, probably due to urinary stagnation and infection leading to stone formation.[7] Polycystic kidney has rarely been associated with malignant tumors,[1] but hypernephroma and Wilm's tumor have been described with the disease.[1,9,10]

Polycystic kidney may be associated with anomalous formation of other organs. In 5% of the cases there is association with cystic liver and in 4% association with splenic cysts[3]. Sixteen and six-tenths per cent of patients with polycystic kidney have intracranial aneurysm and 4% of patients with intracranial aneurysms have polycystic kidney.[11,12] A syndrome of

Continued

bilateral polycystic kidney, polycystic liver, and congenital aneurysm of the basal arteries of the brain has been described by Gates.[1] Cysts have been found in ovaries, uterus, esophagus, cerebrum, cerebellum, pancreas, thyroid, bladder, testes, and epididymis.[1] Association of the disease with aneurysm of the splenic and renal arteries has been described.[13]

McCaughey et al. reviewed Mayo Clinic records from 1946 through 1961 and reported 19 cases of neonatal polycystic kidney disease with brain defect.[14] Dalgaard in his classical review noted seven cases of polycystic kidney associated with brain defect out of 40 neonatal cases.[1] Shands reported simultaneous polycystic kidney and erythroblastosis foetalis in three successive siblings.[15] Campbell in his autopsy series of 72 cases of the disease in infants and children found association of patent foramen ovale in 10, patent ductus arteriosus in five and interventricular septal defect and dextroaortic position in one each.[3]

Pathological Physiology

Lambert subjected two moribund patients with polycystic kidney to intraperitoneal injections of inulin and then demonstrated the presence of inulin in samples of cystic fluid taken immediately after death. He concluded that cystic nephrons in adults retain their function and take part in the formation of urine.[4] This study has been confirmed by Bricker and Patton who performed in vivo experiments in polycystic kidney and on kidneys with simple cysts, by intravenous injections of inulin, P-aminohippurate and creatinine, and found that many of the cysts in five adults and some of the cysts in children were functionally in connection with open nephrons.[5]

Clinical Manifestations

Infancy and Childhood

The disease manifests itself in relation to the degree of renal involvement. It may involve both kidneys completely and cause stillbirth. The kidneys may be very large and cause prolongation of labor and uterine rupture, with respiratory and circulatory difficulties in the infant, endangering his life.

Children manifest striking features: protuberant abdomen and renal facies, described by Potter as consisting of large low set ears, marked inner canthal folds, broad flat nose, microganthia, and often broad, clumsy spade-like hands.[16] Cyanosis and shallow breathing are noted, and respiratory difficulties dominate. Uremia, pain, pyuria, haematuria, and hypertension are noted in children surviving the neonatal period.[14] Fergusson found that the parents of the affected infants appeared normal on clinical and pyelographic examination, an observation implying that the adult form of polycystic kidney is an etiologically different disorder.[17]

In Adults

In the table following are listed the main signs and symptoms of polycystic kidney disease in a series of 366 patients from the Mayo Clinic compared to Dalgaard's series of 350 patients from Denmark.[1,7]

Recently the association of polycythemia with polycystic kidney disease has been described.[18-22] This may be due to increase in erythropoietin activity. It has been reported that erythropoietin is present in greater concentration in the cyst wall than in the cyst fluid, so it is doubtful that cure of polycythemia can be obtained by puncture or aspiration of cysts.[19]

Dalgaard reported four cases of cystic ovaries in 350 patients with polycystic kidney disease.[1] Campbell reported one case of cystic ovaries in his series.[3] A case has been reported from the Massachusetts General Hospital of a 65-year-old female who had polycystic kidney, polycystic liver, pancreatic cysts, and papillary cystadenocarcinoma of one ovary. The other ovary had been removed because of "ovarian cyst" 20 years prior to her death.[28]

TABLE I

Signs & Symptoms	% of Patients (Mayo Clinic) (7)	% of Patients (Dalgaard's Series, Denmark) (1)
Pain	44.5%	59 %
Haematuria	50 %	45 %
Urinary infection: fever, frequency, etc.	33.3%	—
Gastrointestinal symptoms	7.7%	—
Cardiovascular symptoms including hypertension	—	46 %
Bilateral palpable kidneys	51.1%	38.8%
Unilateral palpable kidney	26.8%	22 %
Hypertension	56.1%	28 %
Proteinurea	Majority	74.6%
Pyurea	43.2%	45.7%
Renal insufficiency	47 %	31.5%
Anemia	28.7%	—
Urographic studies	78.8%	—

Urography

Excretory or retrograde urography shows elongation, irregular enlargement, and crescentic deformities (Wine-Glass sign) of calyces. Dalgaard pointed out that the urograms show only the gross anatomical changes, which need not parallel the renal functional impairment.[1]

Prognosis

The infantile type of the disease is rapidly fatal, due to uremia or complications. In the adult type, Dalgaard pointed out that the average age at death was 51.5 years, identical for males and females, and varying between 25 and 85 years. Forty-five per cent (45%) died before the 50th year and 22% after the 60th year.[1] The five-year survival in Simon's series was 56%, while the 10-year survival was 38%.

Causes of Death

In the Dalgaard series 59% died of uremia, 13% from cerebral hemorrhage, 6% from heart disease, and 22% from other causes.[1] Of 193 women with polycystic kidney, 65% were pregnant once or several times; 61% had one or more live births; and only one died during pregnancy.[1]

Treatment

An effective treatment is not available. Whether this disease should be handled conservatively, with surgery utilized only for specific urological

Continued

complications, or whether there is a place for prophylactic surgical decompression to preserve functioning renal tissue is not now known. The urologic complications for which surgery may be required are: nephrolithiasis, infection, associated neoplasm, tuberculosis, hematuria, or intractable pain.[7] In reviewing the literature on decompression of cysts, Dalgaard points out the lack of evidence of improvement, although many felt that decompression improved renal function and the prognosis.[1]

Goldstein in 1951 attempted to compare, in terms of survival, the results in patients having decompression versus those not undergoing surgery.[23] He revised his series in 1960, totalling 57 patients, and reported that those having decompression lived an average 4.9 years longer, compared to 2.3 years for patients not treated surgically.[24] Patton and Bricker in 1954 reported two cases in which they found deterioration in renal function after decompression by surgery.[25]

Seven cases of polycystic kidney, in which unilateral surgical decompression had been carried out and evaluated pre and postoperatively by differential glomerular filtration studies, allowing the nontreated kidney to serve as a control, showed deterioration in function of the treated kidney postoperatively.[26] The best hope in treating this disease appears to be renal transplantation.[27]

Case Summary

This was the second hospital admission for this 28-year-old white female who was admitted 11/19/64 and discharged 11/24/64. Her chief complaint was pain in the right flank beginning the morning of admission.

Family History

The mother has polycystic kidney disease. The maternal grandmother died of the disease.

Past History

The patient had had a similar episode of pain eight years previously. On 2/15/63 she was admitted to Mount Sinai Hospital because of severe colicky pain in the left flank accompanied by nausea, vomiting and chills. The findings at that time were blood pressure 200/140 and hirsutism of the face and thighs. Cystoscopy showed a small calculus at the left ureteral orifice. Admission IVP revealed bilateral polycystic kidneys with a nonfunctioning left kidney. The fundi showed A-V nicking. Urinalysis revealed microscopic hematuria and pyuria, and urine culture grew E.coli. 17-ketosteroids were 13.7 mg. in 24 hrs. Sex chromatin pattern was positive. After being treated with terramycin and analgesics she became asymptomatic. The discharge IVP showed prompt dye excretion bilaterally with disappearance of the obstruction at the left ureteral orifice. She was followed in the Outpatient Department and had several urinary tract infections treated with antibiotics. On one occasion she had gross hematuria.

Gynecological History

She had menstruated three to four times in the past since the age of 13 years. Her last menstrual period was eight years ago. She had been married twice and had had no pregnancies.

Present Admission

Blood pressure was 190/130. There was hair on the face and thighs with a male configuration of pubic hair. BUN 23 mg%, uric acid 7 mg%, white blood count 10,000 cells. Urinalysis: albuminuria 1+, rbc 70-80 and wbc 20-25 per hpf. Urine culture: more than 100,000 colonies of E.coli/cc. Temperature varied between 99.4 and 101. She was treated with analgesics and tetracycline with improvement. Subsequent urine cultures were negative.

She was discharged on the sixth hospital day to be followed in the Outpatient Department. Discharge diagnoses were: (1) polycystic kidney disease, bilateral, adult type, with hypertension and renal insufficiency; (2) chronic pyelonephritis; and (3) Stein-Leventhal syndrome (clinical diagnosis).

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13-28 can be obtained from Grand Rounds Editor at Mt. Sinai Hospital.

For Gout and Gravel

Thomas Sydenham (1624-1689) English internist, known as the English Hippocrates, describes his self treatment for gout and gravel as follows:

"In the morning, when I rise, I drink a dish or two of tea, and then ride in my coach till noon; when I return home, I moderately refresh myself with any sort of meat, of easy digestion, that I like (for moderation is necessary above all things), I drink somewhat more than a quarter of a pint of canary wine, immediately after dinner, every day, to promote digestion of the food in my stomach, and to drive the gout from my bowels. When I have dined, I betake myself to my coach again and when business will permit, I ride into the country two or three miles for good air. A draught of small beer is to me instead of supper, and I take another draught when I am in bed, and about to compose myself to sleep."*

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*Massengill, S. E., M.D.: Sketch of Medicine and Pharmacy. S. E. Massengill Co., Bristol, Tenn.-Va., ca. 1941, p. 56.

Remedies for the Itch*

The itch in man is cured very effectually by using the marrow of an ass, or the urine of that animal, applied with the mud it has formed upon the ground. Butter, too, is very good; as also in the case of beasts of burden, if applied with warmed resin: bull glue is also used, melted in vinegar, and incorporated with lime; or goat's gall, mixed with calcined alum.

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*See Minnesota Med 47:1265, 1964.

Roman Proverb: Fate leads the willing, drags the unwilling.

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Abstracts, Briefs and Commentaries

SEPTIC ABORTION

The article reviews 677 cases of abortion treated between 1957 and 1962 with special emphasis on 95 (14%) cases with sepsis. The typical patient was in her late twenties, had had at least one previous pregnancy, and was in the 11th week of gestation. Two thirds were married. One fourth admitted some attempt to induce abortion.

Seventy-two patients were never dangerously ill and all but two left the hospital within five and one-half days. These two remained longer because of hypofibrinogenemia in one and collagen disease in the other.

Twenty-three patients were classified as seriously ill. These patients had an appropriate history and cardiovascular collapse, whether they were febrile or not. Also severely ill but less obviously so were those with an appropriate history who continued to be febrile and did not improve or got worse despite adequate antibiotics and fluid replacement. Of these ill patients 12 complained of chills and fever, whereas only one fifth of the less ill reported these symptoms. The authors suggest that only the presence of shaking chills and fever was helpful as a prognostic sign. Leucocytosis was not of prognostic value in either the seriously ill or in those less ill.

Patients who were afebrile on admission were treated with antibiotics and early curettage. Although the efficacy of their use was questioned, antibiotics, if used preoperatively, should be given to establish adequate blood levels before uterine manipulation.

Chemically-induced abortion followed by massive collapse precludes surgery. Autopsies among this kind of patient show adrenal hemorrhage and necrosis, acute renal tubular necrosis and pulmonary edema. Dialysis and measures to combat anemia may be life-saving.

Clostridial infection is suspected in the presence of continued abdominal pain associated with muscle aches, crepitus, chills, fever, nausea and vomiting. Surgery must be considered if the patient does not improve after 12 hours of medical management with antitoxins, massive doses of antibiotics, colloid and electrolyte replacement. Curettage may suffice; but if hypotension occurs during the procedure, immediate hysterectomy is recommended. Hyperbaric oxygen and dialysis may be used.

Early hysterectomy (within 12 hours) is recommended when gram-

Continued

negative organisms are present on the cervical smear and hypotension is present.

Stanley Gall, M.D.*
Minneapolis, Minnesota

Barnes, A. B., and Ulfelder, H.: Septic Abortion. JAMA 189:919, 1964.

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*Resident, University of Minnesota Hospitals

APPENDICITIS IN INFANTS

The first comprehensive description of appendicitis was by R. H. Fitz in the *American Journal of Medical Science* in 1886. The extremes of life are largely responsible for the mortality from this disease. Cases in the first two years of life make up about 2 percent of the total cases in children and about 0.2 percent of all cases.

In the past ten years, 17 cases in children under two years old were seen in the Los Angeles Children's Hospital; three of these children were under a year old. The average duration of symptoms on admission was 3.8 days. About a third of the patients had diarrhea.

Fourteen children were operated on after intervals ranging from two hours to five days. All but one had a primary appendectomy; the exception was a simple drainage with a secondary appendectomy. The average stay in hospital was 13 days. The over-all mortality was 12 percent.

A mortality of around 10 to 15 percent for children under two years old seems to be the irreducible minimum until the disease can be recognized earlier. The difficulty of early recognition is illustrated by the fact that 88 percent of the youngest children were found at operation to have a perforated appendix.

Abdominal pain, vomiting and fever are nearly always present in children with appendicitis. Before vomiting and fever start, pathologic involvement of the alimentary tract is suggested by behavior changes, irritability and restlessness as symptoms of pain, and sleeplessness.

Irritability associated with meals is particularly significant, for it is suggestive of painful intestinal peristalsis. Diminished peristalsis accompanied by abdominal distention is an indication of impending perforation. Relief of pain by flexing the hips is a significant sign. A pulse rate of over 180 per minute is a reflection of developing toxicity.

Pain and tenderness are rarely localized in infants. The palpation of a mass on rectal examination is significant. The diagnosis may be made more difficult by the frequent co-existence of respiratory or intestinal infections, or by the masking of symptoms by the administration of antibiotics.

In toxic infants great value is attached to active preoperative preparation, with intravenous fluids, electrolytes, plasma and blood, oxygen, nasogastric suction and antibiotics. No rigid criteria can be laid down for the operation time.

There were two deaths in the 17 cases, but none in the cases treated by operation.

Courtesy of World Wide Abstracts

Liechti, R., and Snyder, W.: Amer Surg 29/2:92.

CERVICAL ESOPHAGOSCOPY

Technic and Use

The use of cervical esophagostomy is an uncommon procedure. The authors state that it has three advantages over gastrostomy: 1, The transperitoneal approach is avoided; 2, The operation is more simple and should take less time; 3, The reflux of a feeding formula is no problem.

Klopp has used this approach in carcinoma of the esophagus, but it cannot be employed if obstruction forbids the passage of a tube. Ketcham uses the method routinely, when indicated, and has performed 168 esophagostomies. However, most surgeons unacquainted with the procedure and its indications prefer gastrostomy. The authors feel that esophagostomy is the choice when tube feeding must be employed over a long period of time (more than one week), as nasopharyngeal discomfort may be severe and cricoiditis may occur. Other indications for the procedure include major surgery for carcinoma involving the tongue, mouth, jaws, etc., and for the acute response to interstitial or external irradiation of the same areas.

The Cleveland Clinic has performed esophagostomy nine times: thrice for carcinoma of the tongue, twice for recurrent squamous carcinoma of the buccal mucosa, twice for malignant melanoma of the maxillary mucoperisteum, and once each for squamous cell carcinoma of the floor of the mouth, and for fibrosarcoma of the maxilla. Two of these patients have been successfully fed by esophagostomy over considerable periods of time, and a third patient will probably continue tube feeding as long as he lives.

Changing the esophagostomy tube is very simply done after one week. When the tube is no longer needed, it may be removed, after which the fistula closes spontaneously in a very short time.

Technic

Local anesthesia lends itself well to this procedure, but intravenous anesthesia may be preferred. A nasogastric catheter is introduced preoperatively. A short incision is made two fingerbreadths above and parallel to the upper border of the clavicle, exposing the anterior border of the sternomastoid muscle. The authors stress the importance of placing the incision as indicated, as the area for the incision in the esophagus is retrotracheal. The tissues are spread and the contents of the carotid sheath are retracted laterally. The finger advances in a posteromedial direction to the body of the seventh cervical vertebra. The thyrolaryngeal structures and trachea lie anteromedial. The index finger feels the previously passed nasogastric tube, and the esophagus is mobilized behind the trachea. With the tube still as a guide, the esophagus is fixed between two sutures. A puncture incision is made between these two sutures and a #16 French Levin tube introduced and advanced to the stomach. The nasogastric tube is removed. The esophageal incision is closed around the French catheter, and the skin incision is brought together around the tube loosely to permit free drainage. The tube is firmly anchored to the adjacent skin.

During the blunt dissection the recurrent laryngeal nerve and the inferior thyroid artery may be exposed.

The above procedure, as described by the authors, appears very simple. Infection with invasion of the mediastinum, usually considered hazardous,

Continued

has been of little or no concern. I have personally observed fatal aspiration pneumonia from regurgitation about a nasogastric tube.

We have never used esophagostomy for feeding, but the seeming simplicity of the procedure and its successful use by others would certainly favor its consideration when indicated.

Stanley R. Maxeiner, Sr.
Minneapolis, Minnesota

Woodburn, Boynton T., Hartnell, Shattuck W., Jr., and Anderson, Robin: Department of Plastic Surgery, Cleveland Clinic Quarterly 31:4, 1964.

TESTICULAR TORSION

Angell reports 16 recent cases of torsion of the testicle. Disturbingly few cases are diagnosed in time to save the organ. Many are wrongly treated, masquerading as epididymitis, and proceed unchecked to testicular atrophy. Two mistaken beliefs are responsible: that torsion is uncommon and that it seldom resembles inflammation.

An appreciation of the anatomical anomaly in torsion of the fully descended testicle is essential for correct diagnosis and treatment. The two layers of the tunica vaginalis, which normally invest the testis alone, extend upward to cover the whole epididymis and the cord, sometimes as high as the inguinal canal.

In addition, the testis is often separated from the epididymis by a lengthened mesorchium, longest at the upper pole, which enables the testis to lie horizontally when the patient is standing. Or it may be that, although the epididymis is closely applied to the testis, the structures of the lower part of the cord are loosely adherent to the epididymis and thus allow the horizontal disposition of the whole testicle. In this series the anomaly was always bilateral, and the general view seems to be that this is the rule.

The patients' ages ranged from eight to 30. The majority were teenagers; one was under 10, three were over 20. The right testis was affected in 11 patients, the left in five.

All the patients seen during an attack were febrile. Temperature ranged from 99° F within a few hours to 103° F later. In one patient abdominal pain and vomiting preceded other symptoms for a whole day, and appendicitis was suspected.

In all the 13 patients examined standing, the unaffected testicle could be seen lying horizontally. This sign could be clearly demonstrated even in cases with much scrotal redness and edema.

In only four of the 16 cases was the correct diagnosis suspected by the doctor who first saw the patient; eight were diagnosed as epididymitis; one was diagnosed as hysteria, one as appendicitis, one as spermatocele, and in one no diagnosis was offered. Moreover, seven were initially diagnosed and treated as epididymitis after admission to a surgical ward, for periods varying from a few hours to 14 days.

Regardless of fever, boys and young men with painful scrotal swellings, however inflamed these may look, should be examined standing up in spite of the additional pain this may cause. If the unaffected testicle is seen to lie in a horizontal plane, no diagnosis but torsion should be entertained.

Courtesy of World-Wide Abstracts

Angell, J.: Lancet 1:7271, 19.

STROKE TREATED SURGICALLY

Young et al. have reviewed 100 cases of extracranial cerebral vascular disease which they have treated surgically. In this group of patients the greatest percentage had artery occlusion in the carotid and vertebral arteries; a few, in the innominate and subclavian. In describing the symptoms the authors referred to remote stroke, progressive stroke, and acute stroke; whereas transient cerebral ischemia constituted 70 per cent of the group.

Physical examination revealed a difference in the pulse and blood pressure in the two arms; positive carotid compression was found in approximately 60 per cent of those tested. Incidentally, there was no fear of this test. The ophthaldynamometer findings correlated with the disease in approximately 50 per cent of the cases, but arteriography was considered to be the only dependable diagnostic method. In addition, the risk was very low.

In the treatment of these patients, 88 received endarterectomy. The best results were obtained in those who presented themselves with episodes of transient cerebral ischemia; it was found that in this group 90 per cent showed improvement.

It appears from this study that in a selected group of individuals presenting particularly transient cerebral ischemia, it should be worth while making studies and performing endarterectomy, which seems to offer considerable benefit. In this group none had subsequent symptoms.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Young, J. D., Humphries, A. W., Wolf, Victor G., Beven, Edwin G., and LeFevre, Fay A.: Extra Cerebral Vascular Disease Treated Surgically. Arch Surg 89:848, 1965.

STENOSES OF ARTERIES OF THE LOWER EXTREMITY

These authors demonstrated that patients with intermittent claudication due to stenosis of the arteries of the lower extremities may have pedal pulses at rest which disappear with exercise. By means of animal experimentation they demonstrated that the major artery to the lower extremity may actually be occluded, and yet there will be a collateral flow and pedal pulses distal to this. They performed intravascular arterial pressure studies in the animals. By artificially stimulating and exercising the lower limbs, they also demonstrated that the flow remains high but that the pulse of the arterial pressures decreases distal to the site of incomplete obstruction. If the obstruction reaches more than 75% of the cross-sectional area of the artery, there is not only a decrease in the pulse distal to the partial obstruction but also a decrease in flow.

They then took the laboratory study into the clinical application by recording the status of 16 patients operated upon, who had between 50 and 83% of the luminal diameter of the femoral arteries obstructed (amounting to 75-97% of the cross-sectional area). These patients had reconstruction of the artery by means of endarterectomy or by venous bypass. Prior to the operation exercise tests were performed on 11 of the patients. All patients prior to exercise had pedal pulses at rest. However, after exercise all the pedal pulses disappeared. After reconstruction of the operation this disappearance of the pedal pulses did not occur. Femoral arteriograms were obtained on four patients following operation which demonstrated patency to the artery. Of the 16 patients who had reconstructive surgery, 12 demonstrated significant improvement six to 66 months after operation.

Continued

The authors concluded that the disappearance of the pedal pulses in a proximal partial constriction is primarily an exaggeration of the normal hemodynamic response, rather than a vasospastic response. The vasodilatation that accompanies exercise decreases the peripheral resistance to increased flow through the major arteries. The decreased peripheral resistance is believed to be in vessels in the large muscles of the leg proximal to the constriction. The authors also felt that the critical stenosis for the human femoral artery appeared to be between 75 and 97% constriction of the cross-sectional area. Patients with such a constriction had loss of pulses and no relief of claudication following lumbar sympathetic block or lumbar sympathectomy following exercise.

This is a rather nice clinical and experimental study. The authors substantiate that the presence of pedal pulses at rest does not necessarily rule out a constrictive lesion at a femoral artery. Indeed from this study, the necessity to exercise the patient and then check the pulses is evident. They also reiterate that, should patients have a complete obstruction with collateral flow and pulsation, obstruction may precipitate problems of ischemia distal to the block. It has been shown by other studies that one of the problems in people who have partial obstruction is that complete thrombosis at the obstruction may occur, with propagation of thrombi into the distal arteries and obstruction of the collateral flow. This lateral type of thrombosis may play a more important part in the resolving ischemia to the limb than the initial site of thrombosis.

Jerome Grismer, M.D.
Minneapolis, Minnesota

DeWeese, J. A., Van de Berg, L., May, A. G., and Rob, C. G.: Stenoses of Arteries of the Lower Extremity. Arch Surg 89:806, 1964.

VERDOGLOBINURIA

In a study of 15 burned patients dying of gram-negative septicemia, particularly of pseudomonas, an urinary pigment- Verdoglobin- was found to be excreted in the urine. The assumption is that the pseudomonas toxin inhibits the reticuloendothelial system from continuing the degradation of hemoglobin into bile-pigment, and that at this stage failure in the continued process allows for buildup and thus urinary excretion of this intermediate pigment. The authors found that the use of fluorescent light many days prior to its recognition in ordinary light permitted advance recognition of this most ominous sign in septicemia. The authors hope that this may be a sufficiently early sign to treat the pseudomonas infection adequately before irreversible damage from the gram-negative septicemia occurs.

This is an interesting observation, and may well be an addition to the constant search for methods of salvage of the extensively burned patient.

J. H. Strickler, M.D.
Minneapolis, Minnesota

Stone, H. Harlan, Martin, J. D., Jr., and Graber, Charles D.: Verdoglobinuria, An Ominous Sign of Pseudomonas Septicemia in Burns. Ann Surg 159:991, 1964.

CHEMOTHERAPY IN INFECTIONS OF THE URINARY TRACT

In a one-year study of 110 patients with urinary tract infections it was found that the patients could be sorted out into four main categories, and that the chief factor in determining the outcome was not the type of therapy but the category in which the patient fell. The diagnostic categories were: (1) Uncomplicated acute pyelonephritis; (2) Complicated acute pyelonephritis (infection with obstructive uropathy); (3) Known chronic bacteriuria (mostly E. coli, but also klebsiella aerobacter, paracolon, and P. mirabilis); and (4) Asymptomatic bacteriuria of unknown duration. In the first category, consisting of women infected with E. coli sensitive to all antibiotics, response to therapy was good. Members of the second category responded well to therapy when the obstructive factor was removed. In the third category, the bacteriuria was eliminated during therapy but recurred, either with the same pathogen or a different one, when therapy was stopped. In the fourth group, mostly females, responses were similar to group 3.

There were 37 females and 73 males, only 12 of whom were under thirty years old. Of the rest, 48 were over sixty-nine; 34 were between fifty and sixty-nine; and 16 between thirty and forty-nine. By table, the authors relate age and sex to the diagnostic category. Drugs used in this series were streptomycin, sulfonamides (not specified), tetracycline, chloramphenicol, kanamycin, and polymixin B. The patients were classified and the bacterial resistance encountered tabulated by diagnostic categories. The clinical response of each patient was studied in relation to antibacterial response.

In groups 1 and 2, only one bacterial strain out of 19 was found resistant (to sulfonamide only). No strain was resistant to any of the other drugs used. Group 3: Known Chronic Bacteriuria (20 strains). In this group six strains were resistant to streptomycin; 14 to sulfonamides; six to tetracycline; and one to chloramphenicol. Group 4: Asymptomatic Bacteriuria (78 strains). In this group 12 strains were resistant to streptomycin; 22 to sulfonamides; 10 to tetracycline; and two to chloramphenicol. All strains, however, were sensitive to kanamycin and all but three to chloramphenicol.

All patients improved symptomatically regardless of therapy or bacteriologic response. Most were free of symptoms in a few days despite persistence of bacteriuria. Only patients suffering gross obstruction and impaired drainage of urine failed to show prompt clinical improvement. The febrile response was also found to be independent of bacterial response as gauged.

The immediate bacteriologic response, unlike the clinical response, was plainly related to the sensitivity of the initial pathogen to the antibiotic administered to the patient. Regardless of the initial effectiveness of the antibiotic against the bacterial offender, however, the final outcome was a function of the diagnostic category of the patient, rather than bacterial sensitivity to the drug.

Courtesy of Medical Abstract Service
Berwyn, Illinois

Lindemeyer, Robert, Petersdorf, Robert: Ann Int Med 58:201, 1963.

After all, the two most important things to learn are, where to find the knowledge you need, and how to get along without it. — Nuggets

Are you as proud of American research as you should be?

Where do the modern drugs you prescribe come from? Between 1941-1964, there were 604 different, new chemical entities made available as drugs to physicians throughout the world. About 74% of these came from the research laboratories of three of the four countries below. If you haven't already done so, take the little quiz.

Now, ready? The answers may surprise you. The United States led all the rest with an amazing total of 369 drugs; Switzerland was next with 44, and Germany next with 33. Italy, a country without patent protection for the inventor, had 0. That's a research score Americans can well be proud of.

research quiz For two decades, three of these four countries have led the world in drug research. Of the 604 significant drugs discovered in the world during this period, how many do you think came from each country? (Answer above)

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☐ GERMANY

☐ UNITED STATES

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Book Reviews

Books are masters who instruct us without rods or ferules, without words or anger, without bread or money. If you approach them, they are not asleep; if you seek them, they do not hide; if you blunder, they do not scold; if you are ignorant, they do not laugh at you. — Richard de Bury

PROCEEDINGS OF THE WORLD FORUM ON SYPHILIS AND OTHER TREPONEMATOSES — **U. S. Department of Health, Education and Welfare, Public Health Service, PHS Publication No. 997, Government Printing Office, Washington, D. C., 1964.**

The World Forum on Syphilis and Other Treponematoses was convened in Washington, September 4-8, 1962, to exchange information and ideas which would be useful in the world-wide struggle to eradicate these infections. As the Foreword points out, the 1500 delegates from over 50 nations included many of the world's authorities on the treponematoses. The Proceedings include scientific papers by specialists on the medical, administrative, and behavioral aspects of venereal disease-control programs.

Since 1958 there has been an alarming increase in the incidence of infectious syphilis in Minnesota as well as all parts of the nation. The problem is expected to continue for the next decade at least, as a result of the 38 per cent population explosion of the young adult age groups. For these reasons, the authoritative articles on such medical aspects as the clinical use of laboratory tests, the problems of biologic false positives, the treatment of early syphilis and the handling of penicillin-allergic reactions are welcome.

A long list of articles on the behavioral sciences related to venereal disease control gives interesting insight on the people concerned with these diseases.

This is a big book which provides a valuable landmark. Copies have been placed in several medical society libraries and the volume can be borrowed from the State Health Department.

R. N. Barr, M.D.
Secretary and Executive Officer
Minnesota State Board of Health

PATIENT CARE AND SPECIAL PROCEDURES, SECOND EDITION — **By Venes and Watson, C. V. Mosby Co., 1964; 228 pages, price $6.25.**

This book is written collaboratively by an experienced nurse and an x-ray technologist for the x-ray technology student. It is an excellent, concise presentation of the more specialized procedures with which the x-ray technologist is involved and the associated rudiments of nursing care with which he must be familiar. The sections dealing with the various categories of emergency and special care patients are particularly pertinent. This book should be read by every x-ray technology student and should be available in the library of every school of x-ray technology.

C. N. Hess, M.D.
Minneapolis, Minnesota

THE OBSTRUCTING ACROMION — **Bernard Diamond, M.D., F.A.C.S., Charles C Thomas. No price listed.**

This is a short (207-p.) monograph on a rather limited orthopedic subject.

The author proposes that resection of the acromion through a proper approach is instrumental in the surgical correction of the following shoulder problems: calcific tendinitis; chronic ordinary cuff tear, chronic massive cuff rupture; lesions of bursa, biceps, and supraspinatous tendons; after fractures of the greater tuberosity.

His impressions are based on his own personal experience with 44 operated cases in which he certainly has achieved remarkably good results.

The book should be of interest to orthopedic surgeons.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

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Special Article

Information and Orders Are Vital

WILFORD E. PARK, M.D.*
Minneapolis, Minnesota

IN THE modern concept of treating the whole patient, through the ministrations of a team of medical and paramedical personnel captained by the attending physician, the nurse still plays a key role. Aside from the physicians and specialists directing the patient's care, no one needs to be better informed than the attending nurse. In this paper we are concerned with the nurse's need to know her patient as quickly and as completely as possible. The "Patient Care Referral" discussed in this paper is designed to facilitate transmission of vital information to her.

The Patient Care Referral form (see front and back illustrations) was developed in Minneapolis in the latter part of 1963 by a committee organized for the purpose as part of a Demonstration Project supported in part by U.S. Public Health Service funds under Contract No. PH 86-62-80 with the Minneapolis Health Department. Since use of this form is rapidly extending throughout the State, every practicing physician and nurse in Minnesota should be familiar with its structure, purposes and potential. The form performs its major service as a communication tool[1] when the patient is being transferred and, therefore, passes from the care of one nurse or nursing service into the hands of another nurse or nursing service. The Patient Care Referral serves equally well regardless of the direction of the transfer and regardless of the diagnosis.

The portion of the form requiring the doctor's attention is on the front, in section III. It is so designed that the attending physician need not write much, but what is written is of great importance to the nurse and vital to the care of the patient. The diagnosis is, of course, a must. Sometimes more than one is indicated. The diagnosis should be specific with dates, such as "Right hemiplegia was aphasia on July 10, 1964."

---

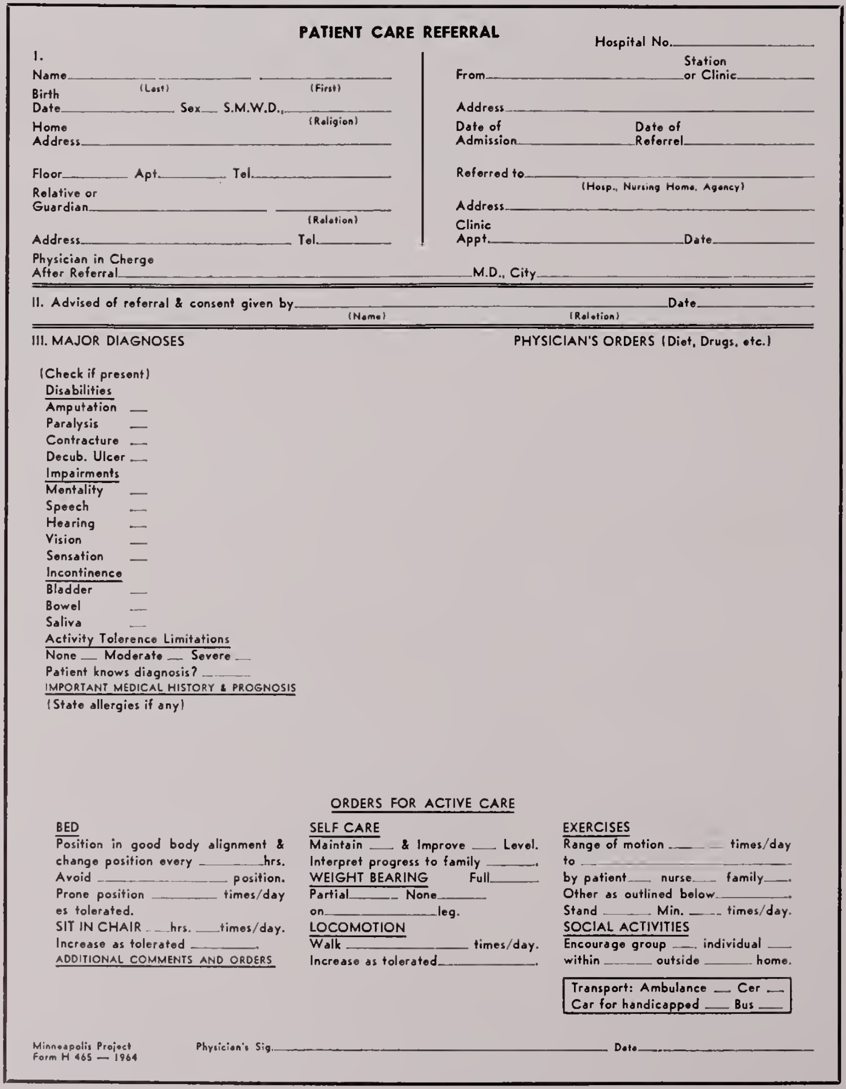
*Director Adult Health, Minneapolis Health Department.

Continued

In some instances past medical history is important. The check list of disabilities enables the physician to indicate common impairments without extensive writing. The doctor's "Orders for Active Care" are not orders for physical therapy; these are orders for nursing to be carried out with the same diligence as giving medicines.

The modern concept of nursing incorporates the philosophy that retention of self-respect and personal dignity and even the will to live are somehow bound up with a patient's ability to take care of himself and to participate in activities with other people. In this concept, nursing does not mean turning away from tender loving care, when it is needed, but it does mean turning its back on coddling, pampering, and fostering of self-pity. The emphasis on patient activity inherent in "active nursing care" gives to the practice of medicine a dynamic revitalizing element which may make the difference between dependent chronic invalidism and a self-sufficient satisfying retirement.

"Active nursing care" is not physical therapy practiced by nurses, and it is no substitute for physical therapy, but it is a supporting role of nursing which may be the sustaining factor making the difference between success and failure in the team approach of physiatrist, nurse and physical therapist. Active nursing-care activities carry with them certain inherent risks which the attending physician is in the best position to evaluate. It is therefore imperative



PATIENT CARE REFERRAL

Hospital No.___

I.

Name___ ___ ___
(Last) (First)

Birth Date___ Sex___ S.M.W.D.,___
(Religion)

Home Address___

Floor___ Apt.___ Tel.___

Relative or Guardian___ ___
(Relation)

Address___ Tel.___

From___ Station or Clinic___

Address___

Date of Admission___ Date of Referrel___

Referred to___
(Hosp., Nursing Home, Agency)

Address___

Clinic Appt.___ Date___

Physician in Cherge After Referral___ M.D., City___

II. Advised of referral & consent given by___ Date___
(Name) (Relation)

III. MAJOR DIAGNOSES

PHYSICIAN'S ORDERS (Diet, Drugs, etc.)

(Check if present)

Disabilities
Amputation ___
Paralysis ___
Contracture ___
Decub. Ulcer ___
Impairments
Mentality ___
Speech ___
Hearing ___
Vision ___
Sensation ___
Incontinence
Bladder ___
Bowel ___
Saliva ___
Activity Tolerence Limitations
None ___ Moderate ___ Severe ___
Patient knows diagnosis? ___
IMPORTANT MEDICAL HISTORY & PROGNOSIS
(State allergies if any)

ORDERS FOR ACTIVE CARE

BED
Position in good body alignment & change position every ___hrs.
Avoid ___ position.
Prone position ___ times/day es tolerated.
SIT IN CHAIR ___hrs. ___times/day.
Increase as tolerated ___.
ADDITIONAL COMMENTS AND ORDERS

SELF CARE
Maintain ___ & Improve ___ Level.
Interpret progress to family ___.
WEIGHT BEARING Full___
Partial___ None___
on___leg.
LOCOMOTION
Walk ___ times/day.
Increase as tolerated___.

EXERCISES
Range of motion ___ times/day
to ___
by patient___ nurse___ family___.
Other as outlined below___.
Stand ___ Min. ___ times/day.
SOCIAL ACTIVITIES
Encourage group ___. individual ___
within ___ outside ___ home.

Transport: Ambulance ___ Cer ___
Car for handicapped ___ Bus ___

Minneapolis Project
Form H 465 — 1964

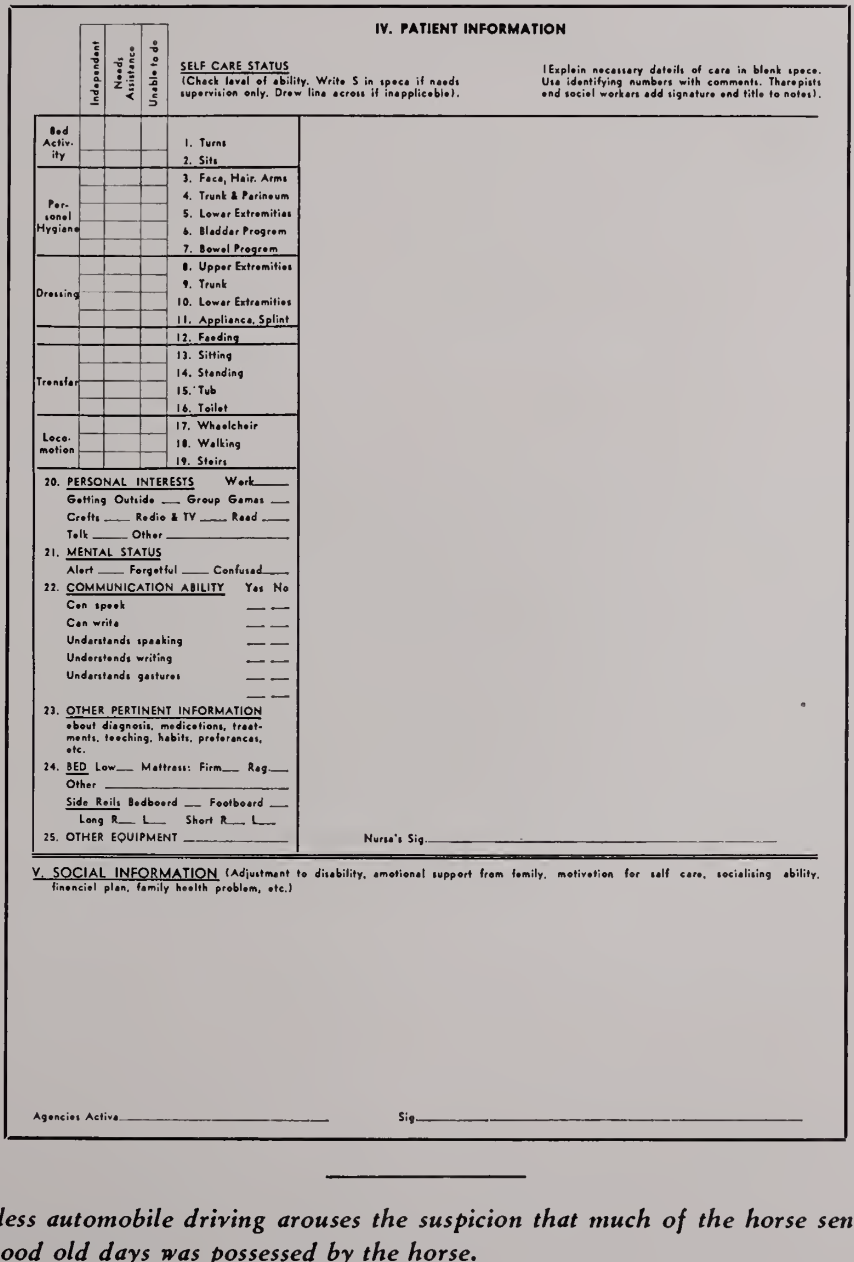
Physician's Sig.___ Date___

that the physician specify when and how much should be undertaken. This is part of the physician's responsibility to prescribe what is best for his patient, but it also defines for the nurse those practices and activities which the doctor is prepared to stand behind and to share legal responsibility for.

The usefulness and success of the Patient Care Referral form is dependent upon the willingness of persons participating in the care of a patient to pass on their knowledge and experience with an individual patient to another physician, nurse, or institution to whom the patient is sent. Physicians and nurses in Minnesota have the first opportunity to prove the worth of this communication tool and through it to demonstrate the high quality of care that can be sustained when a patient passes from one institution or nursing service to another.

Reference

1. Park, Wilford E., M.D. and Anne Hughes, R.N., M.A.: Minneapolis Forges a New Communication Tool. Hospitals, May 15, 1965.



IV. PATIENT INFORMATION

SELF CARE STATUS
(Check level of ability. Write S in space if needs supervision only. Draw line across if inapplicable).

(Explain necessary details of care in blank space. Use identifying numbers with comments. Therapists and social workers add signature and title to notes).

	Independent	Needs Assistance	Unable to do	
Bed Activity				1. Turns
				2. Sits
Personal Hygiene				3. Face, Hair, Arms
				4. Trunk & Perineum
				5. Lower Extremities
				6. Bladder Program
				7. Bowel Program
Dressing				8. Upper Extremities
				9. Trunk
				10. Lower Extremities
				11. Appliance, Splint
				12. Feeding
Transfer				13. Sitting
				14. Standing
				15. Tub
				16. Toilet
Locomotion				17. Wheelchair
				18. Walking
				19. Stairs

20. PERSONAL INTERESTS Work____
Getting Outside ___ Group Games ___
Crafts ___ Radio & TV ___ Read ___
Talk ___ Other ________

21. MENTAL STATUS
Alert ___ Forgetful ___ Confused___

22. COMMUNICATION ABILITY

	Yes	No
Can speak	___	___
Can write	___	___
Understands speaking	___	___
Understands writing	___	___
Understands gestures	___	___
	___	___

23. OTHER PERTINENT INFORMATION about diagnosis, medications, treatments, teaching, habits, preferences, etc.

24. BED Low___ Mattress: Firm___ Reg.___
Other ________
Side Rails Bedboard ___ Footboard ___
Long R___ L___ Short R___ L___

25. OTHER EQUIPMENT ________

Nurse's Sig.________

V. SOCIAL INFORMATION (Adjustment to disability, emotional support from family, motivation for self care, socialising ability, financial plan, family health problem, etc.)

Agencies Active________ Sig.________

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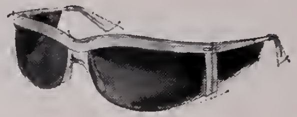

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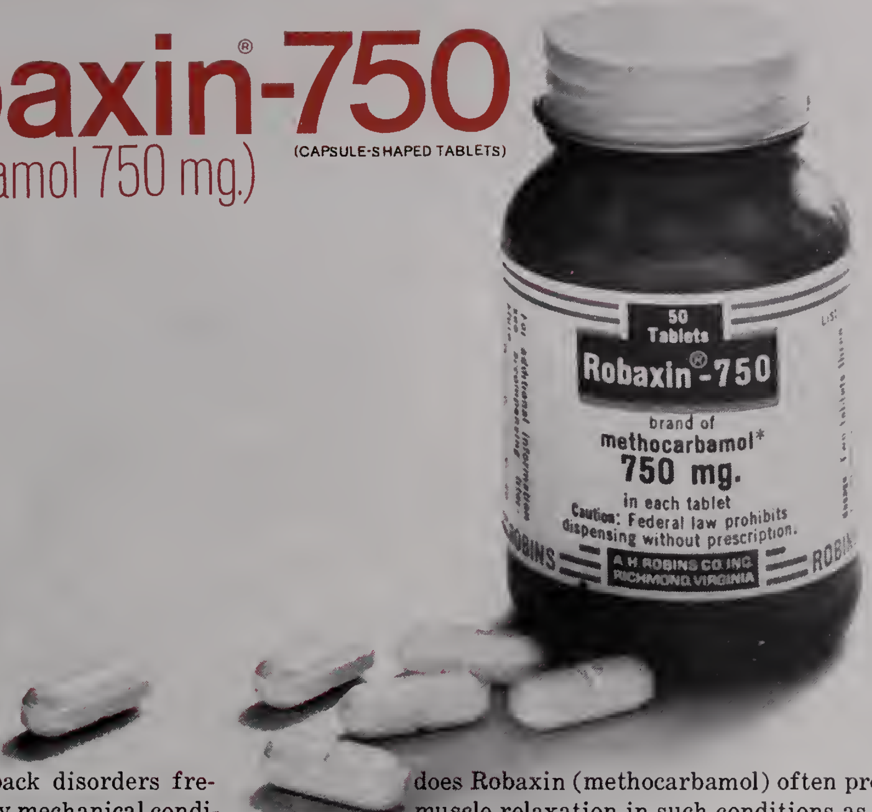

It has been noted that low-back disorders frequently "...are caused by truly mechanical conditions which yield to conservative treatment."[1] Basic to this conservative treatment are bed rest, a board for the bed, and applied heat. In addition, a good muscle relaxant is often helpful, as "...muscle relaxants are useful in chronic as well as acute low backaches."[4]

Robaxin (methocarbamol) has relieved spasm and pain in cases where the patient "had not responded to conservative measures prior to drug therapy."[6] A 100-patient study showed that Robaxin provided greater relief of muscle spasm for a longer period of time without adverse reactions "than any other commonly used relaxants...."[6]

A well-tolerated[7] skeletal muscle relaxant with "specificity of action,"[7] methocarbamol leaves normal muscle tone unaffected. Moreover, there is little likelihood of sedation[7]—a considerable advantage for the patient who must remain active and alert on his job.

Significantly, clinicians advise using a muscle relaxant "early and in adequate dosage."[8] In this regard, Robaxin (methocarbamol)—*particularly in the 750 mg. dosage (2 tabs. q.i.d.)*—offers optimal therapeutic benefits without a significantly increased incidence of side effects. And just as it works well as part of the basic regimen for low-back pain, so also does Robaxin (methocarbamol) often provide muscle relaxation in such conditions as musculoskeletal injury, chronic neurological disorders, and orthopedic situations.

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Robaxisal® (methocarbamol with aspirin) and Robaxisal-PH Tablets (methocarbamol with Phenaphen®).

REFERENCES: 1. Soto-Hall, R.: Med. Sci. *14*:23, 1963. 2. McCarrol, H.R.: Paper read at the Annual Meeting of the American Medical Association, Atlantic City, June 16-20, 1963. See Medical News: J.A.M.A. *185*:39 (July 13), 1963. 3. Gordon, E.J.: Med. World News *5*:54, 1964. 4. Cozen, L.: GP *26*:82, 1962. 5. Larson, C.B.: Postgrad. Med. *26*:142, 1959. 6. Forsyth, H.F.: J.A.M.A. *167*:163, 1958. 7. Weiss, M., and Weiss, S.: J. Amer. Osteopath. Ass. *62*:142, 1962. 8. Rowe, M.L.: J. Occup. Med. *2*:219, 1960.

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History of Medicine

William Beaumont

(Continued from April issue, page 535.)

Although the English physician, William Prout, demonstrated in 1823 the existence of free hydrochloric acid in the stomach and showed that the presence of this acid was necessary for gastric digestion, it was Beaumont who brought the actual process of solution of food into the range of medical practice. This prototype of the true scientific spirit accurately recorded the movements of the stomach during digestion.

The influence of the emotions on the motility of the digestive tract has been known from time immemorial, as instanced in Shakespeare's Othello: "The thought thereof doth, like a poisonous mineral, gnaw my innards," and shown in the Bible: "Joseph made haste, for his bowels did yearn upon his brother." Gen. 43:30. This was only casual observation, but the actual fact of the effect of the psyche on salivary, gastric, and pancreatic secretions was first demonstrated by Beaumont.

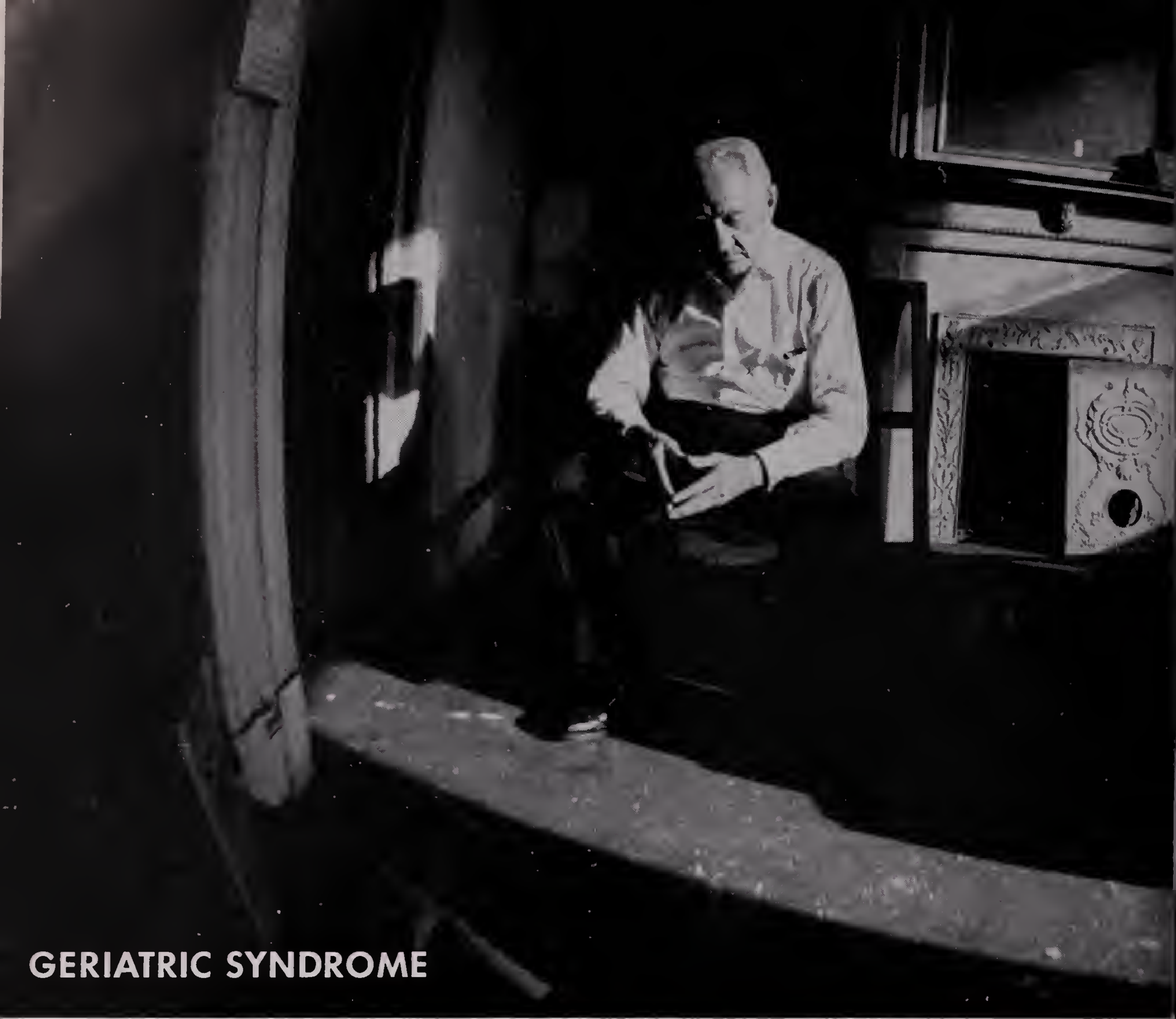
In 1824 Beaumont sent a complete report of his case to Surgeon-General Lovell, who encouraged him to continue his work.

St. Martin was a most recalcitrant human guinea pig. He grew tired of Beaumont's experiments on him, and would run away for long periods of time. The relations between the persistent doctor and his irresponsible subject constitute some of the most amusing episodes in early medical Americana. Many times when Beaumont wished to retrieve the roving St. Martin, he would enlist the aid of officials of the American Fur Co. Correspondence between Beaumont and these officials show the esteem in which he was held and how anxious these men were to help him continue his work. Since the bulk of Beaumont's experiments were completed at Prairie du Chien, names familiar to our region such as Hercules L. Dousman, Ramsay Crooks, and General Henry H. Sibley appear.

"The indomitable experimenter, having now carried out his observations on gastric digestion for eight years, decided to publish a book summarizing his work, and, in 1833 EXPERIMENTS AND OBSERVATIONS ON THE GASTRIC JUICE AND THE PHYSIOLOGY OF DIGESTION by William Beaumont, Surgeon, U.S.A., was printed at Plattsburgh. This work is a classic in physiology. The author described clearly the appearance and properties of gastric juice, proved that the active acid in the gastric juice is hydrochloric acid, pointed out that gastric juice and mucus are separate secretions, demonstrated the profound influence of mental disturbances upon the secretion of the gastric juice, and carried out the first study on gastric motility. He studied further the digestibility of various foods, work which remains today one of the greatest contributions to the subject of dietetics."[5]

Beaumont died in St. Louis April 25, 1853, where he had been in practice since 1839. Shortly before he passed away he uttered these immortal

Continued to page 678



when a change in environment overwhelms him with anxiety

Failing health, financial difficulties, or the death of a spouse are among the reasons why elderly people may be obliged to leave their familiar surroundings. Moving in with children or entering a home for the aged may satisfy practical requirements but can be psychologically traumatic since emotional resilience tends to diminish with age.

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Side effects and precautions: The transitory drowsiness which may occur with hydroxyzine HCl usually disappears spontaneously in a few days with continued therapy, or is correctable by dosage reduction. Dryness of the mouth may be seen with higher doses. Involuntary motor activity has been reported in hospitalized patients on higher than recommended doses. Hydroxyzine HCl may potentiate CNS depressants, narcotics such as meperidine, barbiturates, and anticoagulants. In conjunctive use, dosage for these drugs should be decreased. Because drowsiness may occur, patients should be cautioned against driving a car or operating dangerous machinery. **Parenteral Solution Precautions and contraindications:** This dosage form is intended only for I.M. or I.V. administration and should not, under any circumstances, be injected subcutaneously or intraarterially. When the usual precautions for I.M. injection have been followed, reports of soft tissue reactions have been rare. I.V. administration should be slow, no faster than 25 mg. per minute, and should not exceed 100 mg. in any single dose. Particular care should be used to insure injection only into intact veins; a few instances of digital gangrene occurring distal to the injection site have been attributed to inadvertent intraarterial injection or periarterial extravasation, both of which should be avoided. **More detailed professional information available on request.**

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1. Schleif, R.H.: J.A.PH.A., 46:179,1957 *U.S. Pat. No. 3,062,714

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(Continued from page 675)

words, "Truth like beauty when unadorned is most adorned and in prosecuting these experiments and inquiries, I believe I have been guided by its light."

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1. From Major, Ralph H., A History of Medicine, Vol. II, 1954, Courtesy of Charles C Thomas, Publisher, Springfield, Illinois, pp. 747, 748, 749, 750.

Sir Astley's Daily Schedule

A day in the life of Sir Astley Cooper (1768-1841) was fully as exacting as a day in the life of John Hunter. According to Bransby Cooper, he rose at six, even in winter, dissected until half-past seven or eight, when he had his hair dressed (he wore it powdered with a queue). Then at half-past eight he began to interview his free patients. His breakfast consisted of two rolls, followed by a quick glance at the newspaper. After that he received patients in his consulting room until one. (His servant Charles gave gentlemen preference over ladies, whose time he rated as of little importance; but he could be bribed.) At one o'clock Sir Astley left in his coach, sometimes going out of the house by the back door in order not to run the gauntlet of the disappointed and irate patients still waiting to see him. A very different atmosphere awaited him at Guy's. The steps would be thronged with as many as 100 persons — apprentices, students, hospital staff — who would greet him with great animation and jostle for his recognition. The cavalcade would then tour the wards, Sir Astley courteously explaining any interesting cases. Next he would go to the operating theatre to lecture for perhaps an hour, then out by way of the dissecting room to tour his professional circuit until half-past five or later. After dinner he might fall asleep for ten minutes, but often he would set off again to the hospital to deliver another lecture or to address a medical society. He would be home again by midnight. It was a great day for a great man, who did not conceal that he enjoyed his popularity.*

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*Turner, E. S.: Call the Doctor. St. Martin's Press Inc, New York, 1959.

ANSWER TO WHAT'S YOUR DIAGNOSIS

(From page 610)

The abdomen contained approximately 500 cc. of blood. The right ovary showed a ruptured corpus-luteum cyst measuring about 4 cm. in diameter, from which blood was flowing freely. After excision of the cyst, two units of blood were given, and the patient made an uneventful recovery.

The man whom God wills to slay in the struggle of life He first individualizes.
— Ibsen

Gossip is vice vicariously enjoyed. — Elbert Hubbard

Rural Medical Scholarship

State Physicians Award Rural Medical Scholarship

David Arthur Pope, a University of Minnesota Medical School freshman from Janesville, Minnesota, has been named recipient of the Minnesota State Medical Association's 1964-65 Rural Medical Scholarship.

This $4,000 scholarship, awarded annually to an outstanding freshman medical student, provides $1,000 a year for each of the four years of medical school. In agreement with the terms of the scholarship, Pope has agreed upon completion of his training to practice medicine for at least five years in a rural Minnesota community in need of a physician.

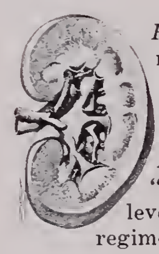
In announcing the award, Dr. Charles G. Sheppard, St. Peter, Minnesota, chairman of the Association's Scholarship and Loans Committee, said the purpose of the scholarship, which originated in 1952, is to provide financial assistance to worthy and outstanding students, and insure a continuing supply of physicians for non-metropolitan areas of Minnesota.

Pope is the fourteenth student to receive the Association's Rural Medical Scholarship. Previous recipients currently practicing in rural Minnesota communities include: Dr. Leland Christenson, Maple Plain; Dr. Myron Doebler, Mora; Dr. Carl Christenson, Clinton; Dr. Vincent Hunt, Red Lake Falls; Dr. LeRoy Mueller, Hendricks: and Dr. George B. Gerstenkorn, Milaca. Dr. Donald Asp, Milaca, is currently completing his internship.

Scholarship winners still attending the University of Minnesota Medical School are Charles Benjamin, Hutchinson; Elton Wing, Jackson; Roland Roy Larter, Lancaster; and William J. Norberg, Barnum.

David Arthur Pope, a University of Minnesota Medical School freshman from Janesville, Minnesota, has been named recipient of the Minnesota State Medical Association's 1964-65 Rural Medical Scholarship.
He is the son of the Rev. and Mrs. W. E. Pope of Lafayette, Minn.

One antibiotic superior to
Tetracycline
Chloramphenicol
Streptomycin
Kanamycin
Polymyxin B
Penicillin G
against Proteus mirabilis and E. coli



Proteus mirabilis is not only the most common cause of *Proteus* infections of the urinary tract, but such infections are often resistant to other antibiotics.[1-4] According to Anderson *et al.*,[5] "When assessed in terms of serum levels attainable with usual dosage regimens, ampicillin was the most effective drug tested against *E. coli* and *P. mirabilis.*" These authors found *Klebsiella-Aerobacter* and *Pseudomonas* organisms relatively insusceptible to ampicillin. With its broad-spectrum coverage of many gram-positive and gram-negative bacteria, absence of toxicity, and slow emergence of resistant strains, PENBRITIN (ampicillin) is a most beneficial and safe drug in treating urinary tract infections—*killing* the pathogens, not just suppressing them.

Dosage: Adults—500 mg. every six hours (higher doses may be required for severe infections). Children—(under 13 years, whose weight will not result in a dosage higher than that recommended for adults) 100 mg./Kg./day in divided doses every six or eight hours for moderately severe infections; 200 mg./Kg./day in divided doses every six hours for severe infections.

Contraindications: (1) Hypersensitivity to penicillin. (2) Infections by penicillinase-producing staphylococci and other penicillinase-producing organisms. *Aerobacter acrogenes*, *Pseudomonas pyocyanea*, and *Proteus morganii* are resistant to PENBRITIN (ampicillin).

Side Effects: Mild effects, such as skin rashes, diarrhea, nausea and vomiting, have occasionally appeared.

Precautions: As with other antibiotics, precautions should be taken against gastrointestinal superinfection. To date, safety for use in pregnancy has not been established.

Supplied: No. 606—Each capsule contains 250 mg. of ampicillin. Bottles of 16 and 100.

References: 1. Hanson, R. J., *et al.*: J. Urol. *79*:1016 (July) 1958. 2. Middletown, J. E.: Brit. M. J. *ii*:497 (Aug. 31) 1957. 3. Today's Drugs, Brit. M. J. *i*:1475 (May 26) 1962. 4. Brumfitt, W., *et al.*: Lancet *i*:130 (Jan. 20) 1962. 5. Anderson, K. N., *et al.*: J.A.M.A. *187*:87 (Feb. 22) 1964.

Kills bacteria—does not just suppress them

PENBRITIN®

Brand of Ampicillin

AYERST LABORATORIES, NEW YORK, N.Y.
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Public Health

Latin American Medicine

Observations of a World-Health Organization Fellow on a Study-Tour in Latin America

CLEMENT C. CLAY, M.D.*
New York, New York

ALTHOUGH A university professor usually cannot boast of great financial reward for his labors, there are certain compensating factors to be taken into consideration. One of them is the opportunity to travel and to study conditions which may assist him in the instruction of his students, American as well as foreign.

In every country we visited, there was an intense interest in the integration of preventive and curative services. In our country we give lip service to such a concept, but we have done relatively little about it. Admittedly the problem is different in countries where medical care is largely the responsibility of the government, as it is in Latin America.

Chile appears to have made the greatest progress in the integration of the services. There the National Health Service was established by law in 1952 to integrate under central government direction: "(a) the services of the voluntary hospitals serving both insured manual workers and indigent persons, (b) the medical services for blue-collar workers, provided principally through centers for care of ambulatory patients, (c) the total public health program with its health centers and stations for various preventive services, and (d) several smaller services.**"

In each Health Area, there are a Base Hospital and Intermediate Hospitals as well as outpatient services, and "Postas Medicas" located in small villages. The outpatient facilities provide all of the services necessary to keep patients *out* of the hospitals as much as possible.

Specialists

Specialists go from the Base Hospital in the Area Poniente in Santiago to the *consultorios* health centers. When a specialist goes to a consultorio, he may see patients as a generalist; but as a specialist he will later see those who are referred to his service at the Base Hospital.

Routine laboratory and X-ray work is done in the consultorios, but complicated procedures are referred to the Base Hospital. All physicians on the staff of the consultorios are on the staff of the Base Hospital. Each is assigned patients for whom he is responsible, and they consider him their doctor. He keeps their medical records in his office. The chief of each service in the Base Hospital must plan and execute the whole program (preventive and curative) for his service in the Area Poniente. He must visit the consultorios and the peripheral hospitals periodically.

The Medical School

San Juan de Dios is a teaching hospital for the Medical School of the University of Chile and the base hospital for the Area Poniente. The chief of each service is a Professor of

Continued

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*Doctor Clay is Director of the Graduate Program in Hospital Administration at Columbia University and was Director of St. Barnabas Hospital in Minneapolis from 1939 to 1941 before going on active duty in the U. S. Naval Medical Corps in World War II.

**Quoted from "Medical Care in Latin America" by Milton I. Roemer, M.D.

the University; but not all of the physicians are on the faculty. Over 300 physicians are attached to the facilities in the Area Poniente (a few work two or three hours a day; most work four hours; some work six hours). There are 20 to 30 residents and 30 to 35 interns. Student nurses from the University have their practical work at the Hospital, and consultorios and laboratory technicians and social workers also come from schools outside the Hospital for practical experience. There is a nine-month course for auxiliary (practical) nurses.

Rural Areas

In the United States, as well as in Latin America, it is difficult to provide adequate medical care to people in the rural areas; physicians, nurses, and other professional and technical personnel are reluctant to leave the big cities. An interesting program has been developed in Colombia by the University of Vallee of Cali. In recognition of its responsibility for the health and welfare of the people in the rural areas, the University formed a committee in 1955 to study medical care needs. The State Government designated the University as the agency for providing complete preventive and curative health services to the people in the County of Candelaria, which has a population of 4700, chiefly Negroes. Most of the people work in the sugar industry, in fields or factories; but a few have shops in town. The average income is about 500 pesos ($50 U. S.) per month.

Throughout the State, all prospective mothers are entitled to prenatal care; preschool and school children are entitled to dental care; all inhabitants are entitled to environmental sanitary services. In Candelaria, however, *all* people are entitled to *complete* preventive and *curative* health services. They pay what they can for those services (50 pesos — $5.00 U. S. for a delivery, for instance). All deliveries in the hospital are done by M.D.s, but midwives do 50% in homes.

Sanitation

The project at Candelaria provides an excellent educational medium for medical students, residents, nurses, and other personnel. Presumably, however, some of those in training should be encouraged to make a career of caring for people outside the large cities. It would seem desirable for other medical schools in Latin America and elsewhere to take an interest in the health needs of the people in rural areas.

Mexico

In Mexico, the Ministry of Health and Welfare has many health centers; but a significant new development has been the creation of a Department of Public Health in the 2,000-bed General Hospital in Mexico City, whose spacious quarters provide rooms for cancer detection, communicable diseases and immunization, a routine chest X-ray unit, offices for the Chief and Assistant Chief and for twelve social workers, and a classroom for health education and other conferences.

The Latin American countries and the United States appear to have one problem in common: the difficulty of interesting the average physician in preventive medicine. Progress has therefore been delayed.

A Latin American "showplace" is the magnificent Centro Medico Nacional del Instituto Mexicano de Seguro Social, a new 2000-bed institution of the "blue collar" Social Security system in Mexico City. This is not truly a "Medical Center" in the sense that the term is used in the United States, but rather a group of seven separate Hospitals with certain supporting facilities. The buildings are handsome and many of them have huge bas-relief murals in stone on their outside walls. Inside, much marble and beautiful woodwork have been used, and there are colorful murals in the lobbies. The equipment is excellent. The facilities, however, are not quite so luxurious as those in the Hospital Central del Empleado in Lima.

Chile

In Chile, the National Health Services has adopted the wise policy of investing in personnel, rather than in buildings. The hospitals and consultorios are substantial structures which are functional but relatively free from frills. An attractive 400-bed general hospital about 55 miles from Santiago was nearing completion, its estimated cost between $1 and $1.5 million U. S. It has been well-planned and should function efficiently and require a minimal amount of maintenance. A comparable building in the United States would probably cost at least $10 million; but labor costs in Chile are far lower.

Peru

In Peru, there is a great contrast in the physical plant and equipment of the hospitals of the Ministry of Public Health, the "blue-collar" Social Security system, and the Beneficencia (somewhat comparable to our voluntary hospitals) on the one hand and, on the other hand, the palatial Hospital Central del Empleado of the "white-collar" Social Security system in Lima. "Stupendous" is a good word to describe this magnificent example of modern architecture. The grounds are beautifully landscaped and the direct approach to the main entrance is across a huge paved plaza. This colossal building with its fourteen stories above two basements is 300 meters long and has a vast expanse of glass. Marble, handsome woodwork, and live plants beautify the mammoth lobbies in the Hospital and Outpatient Department which occupies a one-story wing along with a large, beautiful auditorium. Everything in the building is over-sized. The corridors are nearer sixteen feet in width, rather than the usual eight feet. Each patient's room has only one or two beds and is larger than ordinary; each has its own shower, toilet, and lavatory.

There are about 2,000 visits a day to the medical and surgical clinics. The emergency service has six ambulances and about 180 patients a day. There are about 3,000 employees, including 278 physicians (working six hours a day), 68 interns, 34 dentists, one psychologist, 27 pharmacists, 617 professional and 478 auxiliary (practical) nurses, 113 midwives, and 120 student nurses. Because it is able to pay higher salaries and to offer such superb working conditions, the Hospital Central del Empleado would appear to have no difficulty in attracting physicians and other employees of the highest calibre.

Opportunity for Physicians

In Latin America, the physicians do not have the same reluctance to work for a salary that one observes in the United States. In the countries visited, most of them are employed at a salary for two, three, four, six, or eight hours a day. Because salaries are low, however, even those who work full time (eight hours a day) usually have a private practice in order to earn sufficient income. The consensus seems to be that the salaries are too low, but that there is little hope of their being increased substantially. Since so many of the people are provided with medical care at government expense, there are relatively few who pay for care as private patients. It must be difficult for a younger man to build up a private practice, since patients with the higher incomes are likely to select the well-known physicians.

In some countries young physicians are required to serve in rural areas for a period of time after graduation from medical school but they usually return to the large cities after fulfilling their obligation.

In each of the countries, the hospitals affiliated with medical schools appeared to have well-developed programs for residents in the various specialties. However, it was evident that physicians who could do so would go to the United States, to England, or to countries on the European Continent for postgraduate education.

Everywhere there appeared to be an earnest desire to make available good medical and hospital care to all of the people. The principal obstacles to the attainment of that goal are a great shortage of physicians, nurses, and other professional and technical personnel, the difficulty of correcting geographical maldistribution of available personnel, and a chronic shortage of funds to finance an adequate program of comprehensive health care and to improve nutrition and living conditions.

Don't let yesterday use up too much of today. — Brake Shoe Yardsticks

Of 341 patients with confirmed OB-GYN infections...
320 or 93.8% were treated successfully with Signemycin®

Note:

In 50 cases of serious puerperal and postabortal infections treated with Signemycin, complete cure was observed in 49 patients.* Duration of therapy ranged from three to eight days. Appropriate surgical measures were applied as indicated.

*Heredia Diaz, J. et al.: Medicina (Mex.) 38:308, July 10, 1958.

Condition	No. of Patients	No. Responded to Signemycin
Abortion, infected	45	44
Adnexitis (parametritis)	66	61
Cervicitis	18	18
Endometritis	64	61
Mastitis and breast abscess	44	42
Puerperal sepsis	14	14
Salpingitis	39	34
Other ob-gyn infections	51	46
Totals	341	320 (93.8%)

consistently effective...often when others fail

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tetracycline HCl, 167 mg.; oleandomycin as triacetyloleandomycin, 83 mg. capsules (250 mg.)

Also available as Syrup, Pediatric Drops, and half-strength Capsules

Brief Summary and Bibliography follow.

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Meetings and Announcements

Men are never so likely to settle a question rightly, as when they discuss it freely.
—Macaulay

MAY

Minnesota State Medical Association 112th Annual Meeting, Minneapolis Auditorium, May 17-18. Contact: Harold Brunn, 496 Lowry Medical Arts Building; St. Paul, Minnesota.

Woman's Auxiliary Annual Tea, Lutheran Brotherhood Building, Minneapolis, May 17. Annual meeting, May 18, Minikahda Country Club. Contact: Mrs. F. G. Gunlaugson, 121 West Elmwood Place, Minneapolis or Mrs. R. C. Horns, 4905 West Sunnyside Road, Minneapolis.

Hennepin County Psychiatric Society, May 3, 6:30 p.m., Leamington Hotel, Minneapolis.

Zumbro Valley Medical Society, May 5, Regular Meeting, 8:00 p.m., Plummer Hall, Rochester.

Minnesota Academy of Medicine, May 12, President's meeting, 7:00 p.m., Town & Country Club, St. Paul.

St. Louis County Medical Society, May 13, Executive Comm., 6:00 p.m., St. Mary's Hospital, Duluth. Regular Meeting, 8:00 p.m., St. Mary's Hospital, Duluth.

Minnesota Society of Internal Medicine, May 15, 9:00 a.m., Minneapolis.

Minnesota Society of Clinical Pathologists, May 17, 9:00 a.m., 5:00 p.m., Minneapolis.

Minnesota Chapter, American Academy of Pediatrics, Luncheon meeting, May 17, Minneapolis.

Minnesota Academy of General Practice, Annual May Banquet, May 17, Capp Towers Motor Hotel, Minneapolis. Board of Directors, 7:30 a.m., Capp Towers Motor Hotel, Minneapolis, May 16.

Crippled Children Field Clinics:
May 4 — Detroit Lakes, National Guard Armory
May 11 — Mora
May 13 — Hibbing, National Guard Armory
May 20 — International Falls, Zion Lutheran Church
May 25 — Thief River Falls, Northwestern Hospital

Minnesota Dept. of Health, Div. of Hospital Services, Upper Midwest Hospital Convention, 9:30 a.m.-4:30 p.m., St. Paul Auditorium, St. Paul, May 12-14.

Minnesota Dietetic Assoc., Annual State Meeting, Minneapolis Auditorium, Minneapolis, May 12-14.

Minnesota Academy of Ophthalmology and Otolaryngology, Dinner Meeting (With wives), May 17, Capp Towers Motor Hotel.

Tuberculosis and Health Association of Hennepin County, Board of Directors, 12:00 noon, 1829 Portland Ave., Minneapolis, May 19.

Annual Meeting of the State Medical Society of Wisconsin, May 4, Milwaukee, Schroeder Hotel. Contact: Dr. Joseph Teresi; 561 No. 15th St., Milwaukee, Wisconsin.

JUNE

Annual Meeting of the Medical Library Association, May 30-June 3; Bellevue-Stratford Hotel, Philadelphia. Contact: Medical Library Association; 919 No. Michigan, Chicago.

American Cancer Society Scientific Meeting, Drake Hotel, June 16, Chicago. Symposium on "Hormones and Chemotherapy for Cancer" is open to all members of the medical and dental professions. Contact: Society, 219 E. 42nd St., New York.

American Physical Therapy Association Annual Meeting, Cleveland, Ohio, June 27-July 2, Sheraton-Cleveland Hotel. Contact: Association, 1790 Broadway, New York.

Southern Minnesota Academy of General Practice, Seminar, 3:45 p.m., Fairmont, June 1.

St. Louis County Medical Society, Executive Comm., 6:00 p.m., St. Luke's Hospital, Duluth, and Regular Meeting, 8:00 p.m., June 10.

Minnesota Dept of Health, Div. of Special Services, 8:30 a.m.-4:00 p.m., Continuation Center, Univ. Campus, Minneapolis, "Handicaps of Premature & New Born," June 10-11.

Minnesota Assoc. for Retarded Children, Annual Conference, Macalester College, St. Paul, June 11-12.

Tuberculosis and Health Association of Hennepin County, Annual Meeting, 12:15 p.m., Capp-Towers, Minneapolis, June 16.

American Medical Association, Annual Convention, New York, June 20-24.

Continued on page 689

Of 1,028 patients with confirmed respiratory infections... 954 or 92.8% were treated successfully with Signemycin®

Note:
Hammerl* selected his patients for treatment with Signemycin on the basis of demonstrated bacteriological resistance to other antibiotics or failure of previous therapy. Of 100 patients with various respiratory tract infections, 95 responded to Signemycin. Pathogens isolated included staphylococci and *Diplococcus pneumoniae.*

*Hammerl, H.: Wien. Med. Wschr. 108:629, July 26, 1958.

Condition	No. of Patients	No. Responded To Signemycin
Abscess, pulmonary	17	16
Bronchiectasis	19	13
Bronchitis	286	267
Bronchopneumonia	192	179
Empyema	12	11
Pneumonia, lobar	150	146
Pneumonia, other febrile	160	150
Various infected pneumopathies	192	172
Totals	1,028	954 (92.8%)

consistently effective...often when others fail

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tetracycline HCl, 167 mg.; oleandomycin as triacetyloleandomycin, 83 mg.

capsules (250 mg.)

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Brief Summary and Bibliography follow.

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In Minneapolis . . .

WHERE MINNESOTA DOCTORS WILL BE IN '65

Several innovations will mark the 112th Annual Meeting of the Minnesota State Medical Association which is scheduled for May 17 and 18 at the Minneapolis Auditorium.

One of them relates to a change in the customary schedule of the House of Delegates' meetings. The first session will be convened at 10:00 A.M. on Sunday, May 16, in accordance with a plan proposed by the Speaker of the House, Dr. John L. Falls of Red Wing, and approved by the Council at its February 28 meeting. Opening addresses and reports will be given at the morning session.

The change was occasioned by the fact that a special report must be considered by the full House this year, in accordance with a resolution adopted at the 1964 session. The Sunday afternoon session will take the form of general attendance at a meeting of the Reference Committee on Medical Economics Reports for the purpose of considering the special report.

Other reference committee reports, and the usual election of officers will take place at the final session on Tuesday, May 18 at 9:00 A.M.

The scientific sessions which open on Monday, May 17, will feature a far-ranging series of discussions and panels, all of them concentrated in two days of meetings. The two-day convention is another innovation tried for the first time this year, and it is the hope of the Committee on Scientific Assembly that attendance will be outstanding for both days of the meetings.

Monday's events include extensive discussions on the use of anticoagulants, on fractures in children, on functional disease and on alcoholism; also an important panel on medicine and religion.

Tuesday's program will be given by illustrious alumni and faculty members of the University of Minnesota. It will constitute the State Association's observance of the 75th anniversary of the founding of the Minnesota Medical School. Preceding the program, Dr. J. M. Stickney, President of the Association, will give a special tribute to Medical School accomplishments. Among the distinguished former Minnesotans who will speak are Dr. Raymond D. Pruitt, Chairman and Professor of Internal Medicine at Baylor University, Houston; Dr. George E. Moore, Director of the Roswell Park Memorial Institute, Buffalo, New York; and the Honorable Warren E. Burger, Judge of the United States Court of Appeals for the District of Columbia. Judge Burger will talk about the doctor in court.

Four and one half credit hours for each day have been approved for members of the Minnesota Academy of General Practice who attend.

Visiting speakers and local authorities will act as discussion leaders for five Round Table Discussion Luncheons on Monday and six luncheons on Tuesday, all at 12:15 P.M. at the Capp Towers Motor Hotel. Other special events will be the annual New Members, County Officers and Delegates dinner on Sunday, May 16, at 6:00 P.M.; a Fire-

Continued

Of 425 patients with confirmed G.I. infections... 387 or 91.1% were treated successfully with Signemycin®

Note:
Loughlin and co-workers* achieved cure (absence of parasites) in all 100 of their patients with *chronic amebic colitis*. Feces became negative in all within the planned ten-day period of Signemycin administration. Upon re-examination of the feces six weeks later, the offending pathogen *(E. histolytica)* had reappeared in only 7 cases.

*Loughlin, E. H. et al.: Antibiot. Med. 7:739, Dec., 1960.

Condition	No. of Patients	No. Responded to Signemycin
Amebiasis	237	222
Cholecystitis and cholangitis	105	97
Enteritis	41	31
Peritonitis	15	14
Various, including pancreatitis, appendicitis and colitis	27	23
Totals	425	387 (91.1%)

consistently effective...often when others fail

Signemycin®

tetracycline HCl, 167 mg.; oleandomycin as triacetyloleandomycin, 83 mg. capsules (250 mg.)

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side Conference on Chest Diseases on Monday night at 9:00 P.M., and the Annual Banquet of the Association which will be the final event and climax of the meeting, all at the Capp Towers. Entertainment plus the annual presentations will constitute the program.

Sports events begin at 10:00 A.M. on Sunday with the annual golf tournament at the Hazeltine National Golf Club in Chaska; and the annual skeet and trap shoot at the Twin City-Hopkins Gun Club. A sports dinner, open to all sports enthusiasts, will follow the play at the Hazeltine club.

The Annual Meeting of the Woman's Auxiliary to the Minnesota State Medical Association will begin at 9:15 A.M. at the Minikahda Country Club on Excelsior Boulevard. A program of reports, presentations and election of officers will be followed by the annual luncheon, also at the club, at which the national Auxiliary president, Mrs. William H. Evans of Youngstown, Ohio, will speak; and there will be an AMA-ERF pageant with Auxiliary members acting as models. The Tuesday program will be preceded, on Monday, by the Executive Board meeting at 10:30 A.M. at the Curtis Hotel, with luncheon; and the annual tea to which all doctors' wives are invited, to be held at the Lutheran Brotherhood Building in Minneapolis.

Programs for all meeting events have been mailed to all members and to physicians in surrounding areas. A large registration is expected and registration cards which went with the programs should be returned promptly.

Announcements continued from page 685

Postgraduate Courses at Vienna, Austria

The American Medical Society of Vienna in connection with the Vienna Academy of Medicine has available courses and seminars for practical medicine. Practical sessions and actual patient examination and treatment, surgical operations, round table discussions and grand rounds are part of these seminars. These seminars are arranged individually for any single visiting doctor or any group, for a few days or a month. Upon completion special certificates are issued for studies of three months duration. All these contacts are with English speaking members of the clinics. The cost of these courses range from $1.00 to $6.00 per hour for seminars, and up to $70.00 a month. Life membership in the Society is $30.00 and associate membership $10.00.

The club headquarters of the Society are situated in the University section of Vienna and in close proximity to the University Clinics. It offers every possible amenity to the visiting doctor. The club rooms and extensive library has become a study center for English speaking doctors in Europe. The visiting physician will find Vienna a revived cultural capital. The city surroundings are pleasant during all seasons. Water sports, golf, and during the winter all skiing and Alpine sports centers are within easy reach of the city. Hotel accommodations are available in all price classes to American standards. Time spent there under these auspices represents a bona fide medical continuation training and expenses incurred in connection with these seminars are deductible according to the Internal Revenue Service ruling.

Further information may be obtained by writing to the Secretary of the American Medical Society of Vienna, Universitaets-strasse 11, Vienna 1, Austria.

* * *

A symposium on Cardiac Emergencies will be held in the auditorium of the Ramsey County Medical Society, Lowry Medical Arts Bldg., St. Paul on June 4 and 5. No fee for registration. Open to all physicians. Laboratory Demonstrations will be included as part of course. Sponsored by Department of Medicine, Ancker Hospital, Minnesota Heart Association, State Health Department and St. Paul City Health Department. Contact: James Hammarsten, M.D., Ancker Hospital.

* * *

Three-day course directed to surgically oriented physician will be held at the University of Wisconsin's Medical Center, Aug. 26-28. Aspects of cardiovascular surgery, biliary tract surgery, general abdominal surgery will be presented. Write: The University in Madison.

* * *

Minneapolis Ophthalmological Society will hold a course in Practical Contact Lens Fitting, May 2, St. Barnabas Hospital School of Nursing in Minneapolis. Contact: Robert Fink, M.D., 1921 Medical Arts Bldg., Minneapolis.

The attempt to combine wisdom and power has only rarely been successful and then only for a short while. — Albert Einstein

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Side Effects: Glossitis and allergic reactions, as well as severe anaphylactoid reactions, have been reported as rare side effects. Should significant reaction or idiosyncrasy occur, discontinue medication and institute countermeasures. Use of tetracycline during the last trimester of pregnancy, neonatal period and early childhood may cause discoloration of developing teeth. Reduce usual oral dosage and consider serum level determinations in patients with impaired renal function to prevent possible liver toxicity due to excessive accumulation of antibiotic in the serum.

Precautions: Overgrowth of nonsusceptible organisms may occur. In such cases, discontinue medication and institute appropriate specific therapy as indicated by susceptibility testing. Aluminum hydroxide gel given with antibiotics has been shown to decrease their absorption and is contraindicated. The coloring agents used in Signemycin Syrup and Pediatric Drops may produce red discoloration of stools.

Triacetyloleandomycin, a constituent of Signemycin, administered to adults in daily oral doses of 1.0 Gm. (3 Gm. Signemycin) for periods of more than ten days may produce hepatic dysfunction and jaundice. In the rare patient who requires this high dosage level of Signemycin initially, liver function should be carefully followed and dosage should be reduced, as promptly as possible, to the usual recommended range of 1.0 to 2.0 Gm. per day. Therefore, Signemycin is recommended primarily for the treatment of acute or severe infections, with treatment restricted to a ten-day period. If clinical judgment dictates continuation of therapy beyond ten days, serial monitoring of the liver profile should be carried out, including BSP, transaminase, and cephalin flocculation tests. Changes observed in liver function were reversible following discontinuation of the drug.

Formulas: Capsules: 250 mg. Signemycin (167 mg. tetracycline HCl and 83 mg. oleandomycin as triacetyloleandomycin).

Capsules: 125 mg. Signemycin (83 mg. tetracycline HCl and 42 mg. oleandomycin as triacetyloleandomycin).

Syrup: 125 mg. Signemycin (tetracycline equivalent to 83 mg. tetracycline HCl and 42 mg. oleandomycin as triacetyloleandomycin) per 5 cc.

Pediatric Drops: 100 mg. Signemycin (tetracycline equivalent to 67 mg. tetracycline HCl and 33 mg. oleandomycin as triacetyloleandomycin) per cc.

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Note:

The high rate of response to Signemycin in these cases is noteworthy because the totals include many patients with difficult-to-treat infections, many whose infections had proved resistant to other agents, and many who had been treatment failures on other therapy.[1-87] In addition the following criteria were used for the cases cited: (1) only published results were used (2) results were confirmed by clinical and/or laboratory findings (3) patients were cured, not "improved" (4) dosage conformed with current recommendations in the United States (5) no other anti-infective agents were used concomitantly (6) no instance of prophylactic use was included in these tabulations.

Condition	No. of Patients	No. Responded To Signemycin
Ear, nose and throat infections	507	465
Respiratory infections	1,028	954
Gastrointestinal infections	425	387
Genitourinary infections	748	684
Skin and soft-tissue infections	1,088	1,036
Bone and joint infections	71	64
Deep-seated or generalized infections	257	251
Obstetrical & gynecological infections	341	320
Miscellaneous conditions	592	570
Totals	5,057	4,731 (93.5%)

consistently effective...often when others fail

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Medical Economics

Give Yourself Ample Time

In recent years, great emphasis has been placed upon the importance of one's having adequate capital for income at retirement age. Too little importance, however, has been attached to the achieving of a degree of financial independence in advance of retirement age. This is a grave error.

The years between 45 and 64 have become the truly critical ones in a man's financial life. The young man in his thirties who fails to start saving and investing, contenting himself with the notion that there still is "plenty of time," is operating under a grave delusion. Facts indicate that if the "average" person has not accumulated a reasonable amount of capital by age 45, he is unlikely ever to do so. He has started his search for financial security at too late an hour, and the odds are strongly against his gaining sufficient momentum to make up for lost time.

There are two reasons for believing that a man must begin saving and investing early. One is pure arithmetic, and the other reflects the economic and psychological influences under which we live. The arithmetic is simple. We all know that a dollar saved today is worth considerably more than a dollar that we may save 20 years in the future. Today's dollar, invested wisely, will earn more dollars as the years go by.

Investments that will Accumulate to $1,000 at Age 65

(Assuming a 5% compound interest factor)

$142	invested at age	25
$181	invested at age	30
$231	invested at age	35
$295	invested at age	40
$377	invested at age	45
$481	invested at age	50
$614	invested at age	55
$784	invested at age	60

Stated another way, $181 invested at age 30 will grow to $1,000 at age 65, assuming a five per cent increment. The same $181 invested at age 50 will grow only to $375. If invested at age 60, it will grow merely to $232.

It is obvious from these figures that one dollar invested at age 30 will accomplish as much as two dollars invested at age 45, and as much as nearly $4.50 invested at age 60. As the rate of return and appreciation goes up, the value of early investing is magnified.

The greatest allies a man has in the capital-building process are (1) time and (2) return on capital. Both must work for him if he is to accomplish his financial goals. Take away time, and capital is denied the opportunity to grow. If the burden is placed upon capital — i.e., if too little money must achieve too much too soon — disproportionate risks must be undertaken.

Take away yield, the opportunity to invest productively — and only a very few men could set aside enough from their earnings to achieve any degree of financial independence. It is capital at work, not men at work, that brings eventual financial independence. True, men must work and save in order to provide the basic capital, but afterwards, the degrees of financial independence they attain will be directly proportional to the time that remains for the capital to grow.

Let's call a spade a spade! Can any man say that he is financially successful, whatever his income from his profession, when he has little or no income to report on page 3 of his Federal Income Tax Return? A man of 45 should be well on his way toward accomplishing his financial objectives — not just starting his pursuit of them.

The individual who contents himself with resolving to start his investment program *after* he finishes equipping his home luxuriously, *after* he has paid for his children's education, and *after* he has toured Europe and realized his other recreational dreams, is due for a rude awakening. Both time and simple arithmetic are building up strong odds against him.

The ingredients for success are an early start and tenacity in carrying out one's plan. These things will assure accomplishment; complacency and postponement will assure failure.

Delay

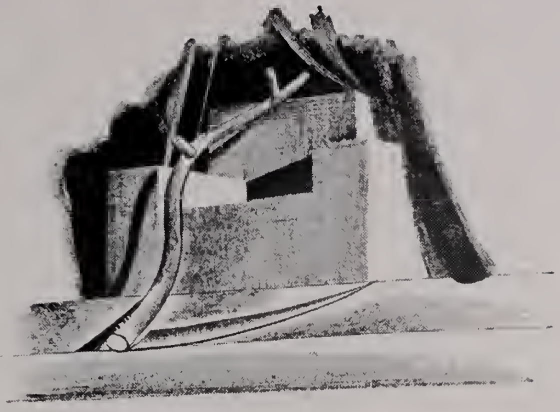
He slept beneath the moon,
He basked beneath the sun;
He lived a life of going-to-do
And died with nothing done.
— *James Albery*

Breast cancer can be highly curable if it is detected early, through regular examinations. Yet, despite all efforts in cancer education and improvements in treatment techniques in the last 30 years,

THE NUMBER OF BREAST CANCER DEATHS PER 100,000 WOMEN IN THIS COUNTRY HAS NOT DECLINED.

While research continues to seek new answers, it is imperative that greater efforts be made to detect breast cancer early and to get women to their doctors when chances of cure are best. That's why the American Cancer Society is encouraging its Divisions across the country to carry out special breast cancer educational programs. Newest of these are demonstration projects in which physicians in a community volunteer one day to giving breast examinations and to teaching hundreds of women breast self-examination. Breast cancer is one of the major cancer problems which we face and which together, doctor, we must try to resolve through intensified research and educational efforts.

AMERICAN CANCER SOCIETY



In Memoriam

What a superlatively grand and consoling idea is that of death! Without this radiant idea, this delightful morning star, indicating that the luminary of eternity is going to rise, life would, to my view, darken into midnight melancholy.

—John Foster

J. LAWRENCE NOBLE

Dr. J. Lawrence Noble, 56, St. Paul physician and surgeon, died at his home, March 7th. He was born in St. Paul and attended the University of Minnesota medical school.

Dr. Noble was a member of the American Medical Association, Minnesota State Medical Association, Ramsey County Medical Society, American Academy of General Practice, Bethesda Lutheran hospital staff, and was on the board of managers of the Bethesda infirmary. He was president of the Gustavus Adolphus church council, member of the board of trustees of the Gustavus Adolphus church and treasurer of the board of social ministry of the Minnesota Synod of the Lutheran Church in America.

He is survived by his wife, a son and a daughter.

CARL A. WITHAM

Dr. Carl Albion Witham, 83, Edina surgeon, died March 10th. He was born in Glouchester, Maine and graduated from the University of Minnesota medical school.

Dr. Witham practiced medicine for sixty years and was an honorary staff member at Methodist hospital and an active staff member at Lutheran Deaconess hospital. He was a member of the Hennepin County Medical Society and American Medical Association and a life and 50 Club member of the Minnesota State Medical Association.

He is survived by a daughter and two sons.

LOUIS A. NELSON

Dr. Louis A. Nelson, 89, long-time St. Paul physician, died March 10th. He was born at Lanesboro and had been a St. Paul resident for eighty-five years. Besides his own medical practice, Dr. Nelson was eye surgeon for the Northern Pacific Beneficial association for forty-two years.

He graduated from the University of Minnesota medical school in 1896 and was a member of the American Medical Association, Ramsey County Medical Society, life member of the American Academy of Ophthalmology, and a 50 Club member of the Minnesota State Medical Association.

He is survived by his daughter, and a son, Dr. Louis Nelson, Jr. of St. Paul.

DAVID M. SIPERSTEIN

Dr. David M. Siperstein, 67, Minneapolis pediatrician, died March 11th. He was an associate professor of pediatrics at the University of Minnesota and chief of staff of pediatrics at Mt. Sinai hospital.

Dr. Siperstein was a member of the American Academy of Pediatrics, the Minnesota Pediatrics Society, Minnesota State Medical Association, American Medical Association, Hennepin County Medical Society, Alpha Omega Alpha and Sigma Psi scientific societies.

He is survived by his wife and two sons, one of whom is Dr. Marvin D. Siperstein of Dallas, Texas.

ĕth´ĭks

Ethics. Where have they gone?

Ethics, says the dictionary, is "the science of human duty; moral science."

In today's world, so complicated with gadgetry and machines that we often lose sight of others and of our own best selves, it isn't always easy to keep "human duty" in mind.

As life gets more complicated, men lose their sense of identity, value and purpose. Life, in a sense, becomes "cheap" and "unimportant." And with that, it becomes ever easier to take the easy way, to ignore the principles of right—and our human duty to others.

The one place where human values are kept in proper focus is where you worship. Nowhere is the individual more valued. *And if you care*, the place where you worship can become, with your help, a rallying point for lifting all the deteriorating values you see around you. Worship this week—and put your faith to work *all* week.

Worship this week

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RELIGION IN AMERICAN LIFE

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Physician's Diary

It is good discretion not to make too much of any man at first, because one cannot hold out in that proportion.—Bacon

Dr. W. G. Workman, 77-year-old Tracy resident and civic leader and practicing physician for more than a half century, has been named "outstanding senior citizen" of Lyon County by a selection committee. **Dr. M. A. Burns**, 90-year-old Milan physician, was named "outstanding senior citizen" of Chippewa County. These gentlemen competed against entries from other counties in the state to name the State of Minnesota's "outstanding senior citizen."

* * *

On January 29, 1965 a group of physiatrists met in Minneapolis to form the Minnesota Physiatric Society. Elected as officers were: **Dr. Bror S. Troedsson** of Minneapolis VA Hospital, president; **Dr. G. Keith Stillwell** of the Mayo Clinic, vice president; and **Dr. John E. Quast** of the Minneapolis VA Hospital, secretary-treasurer. The purposes of the organization are to promote optimal care for physiatric patients, to further education of physiatrists and affiliated groups, and to encourage research in areas of interest to physiatrists.

* * *

The following physicians were recently certified as Diplomates of the American Board of Pathology: **Drs. Wayne A. Chadbourn, Robert L. Strom** and **Patrick C. J. Ward** of Minneapolis; **Dr. Richard P. Lynch** of St. Paul; and **Dr. Mehdi Orandi** of Fergus Falls.

* * *

At the recent meeting of the Minnesota Radiological Society, the following officers were named: **Dr. L. Fink** of St. Paul, president; **Dr. Joseph Jorgens** of Fort Snelling, vice-president; and **Dr. Edward A. Peterson** of St. Paul, secretary-treasurer.

* * *

Dr. L. H. Rutledge of Detroit Lakes has received special recognition for his achievements by being named in the 1964-65 edition of "Who's Who in the Midwest." **Dr. Henry Alexander Korda**, physician and surgeon at Pelican Rapids, was also named for this honor.

Dr. Mathew Yelle was recently given the Distinguished Service award by the Anoka Junior Chamber of Commerce, and **Dr. Arnold S. Leonard** was the winner of the Golden Valley Jaycees Outstanding Citizen award.

* * *

The medical staff of Fairview hospital, Minneapolis, elected in March **Dr. Robert R. Cooper** hospital chief-of-staff. Other officers elected were **Dr. M. S. Belzer**, chief-of-staff-elect; **Dr. John Hartwig**, secretary; and **Dr. Henry Brand**, treasurer.

* * *

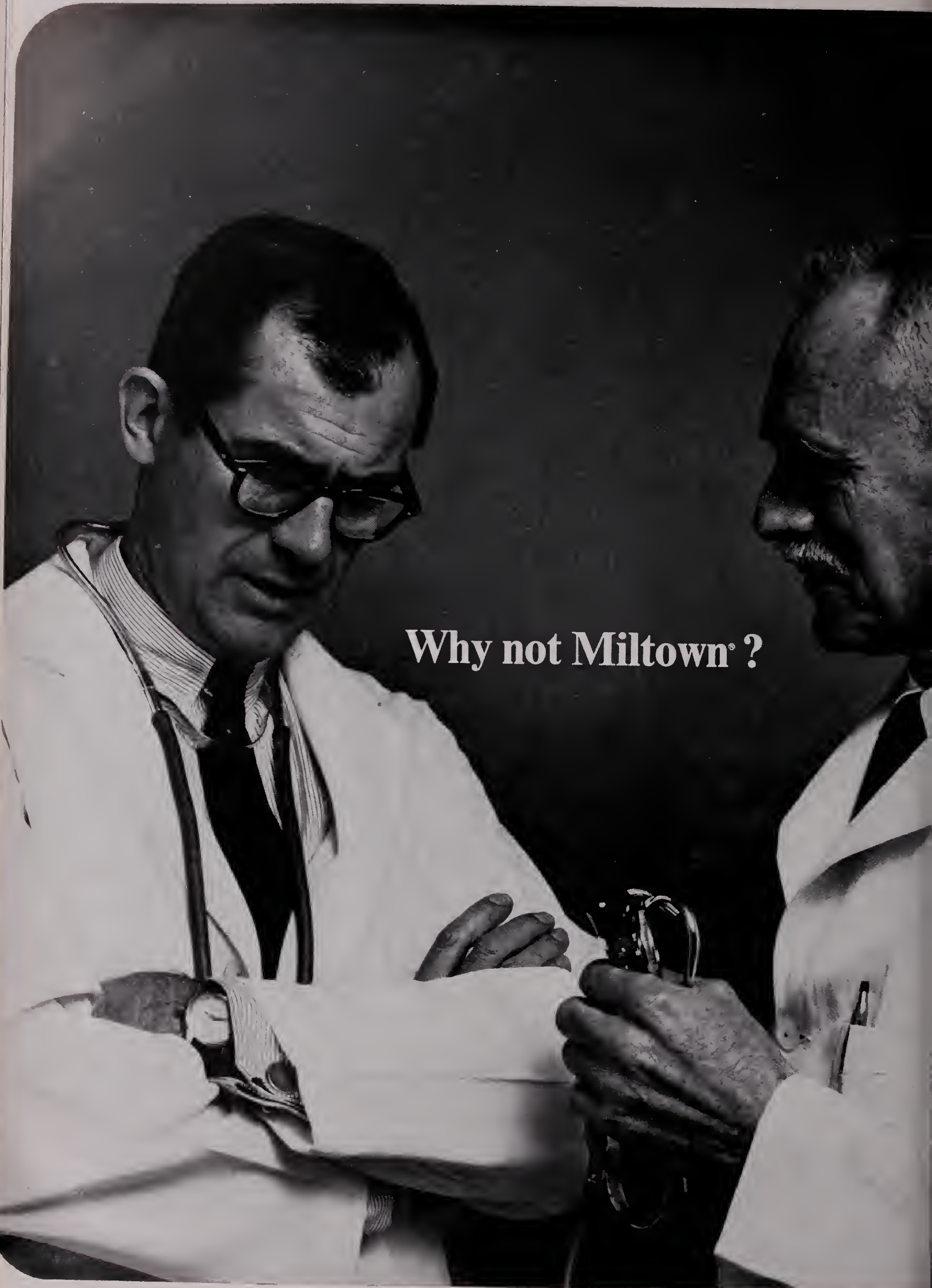
Dr. Arnold Larson of Detroit Lakes has retired from the practice of medicine after completing thirty years of practice in Detroit Lakes and forty-seven years as a Minnesota doctor. Dr. Larson stated in a recent interview that "It has been a most rewarding career."

* * *

NEW LOCATIONS: **Dr. L. A. Whitesell, Jr.** of Shakopee has opened up his own practice in Chanhassen . . . **Dr. Robert L. Hegrenes** and **Dr. Robert Cowger** of St. Paul will join the River's Edge Medical Clinic in Farmington in July . . . **Dr. Thomas C. Leach** of Minneapolis has joined the staff of the Babbitt Medical Clinic . . . **Doctors Edward C. Maeder** and **Clark A. Shattuck** of Minneapolis have opened up a new suburban office in Crystal . . . **Dr. Richard J. Snyder**, an army major stationed at Fort Benning, has been named to the staff of the Mankato Clinic effective June 1 . . . **Dr. Robert J. Knip** has begun a practice of his own in Ortonville.

* * *

Dr. Robert H. Ebert of Minneapolis has been chosen dean of the Harvard medical school. He will succeed Dr. George P. Berry, effective July 1. Dr. Berry is retiring.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Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Usual adult dosage: One or two 400 mg. tablets three times daily. Doses above 2400 mg. daily are not recommended.

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FOR SALE: White frame Rambler with beautiful natural stone trim suitable for medical clinic. Large lot located on a busy corner in both business and residential area on County Road #3 in Hopkins, Minnesota: Write: Mrs. Carl Lillvik; 145 20th Ave., South; Hopkins, Minnesota.

WANTED: General practitioner or physician interested in internal medicine to join rural clinic in Northwest Minnesota. Excellent hospital facilities, good school, churches, golf course, fishing and hunting. Write: MINNESOTA MEDICINE — 308; 496 Lowry Medical Arts Building; St. Paul, 55102.

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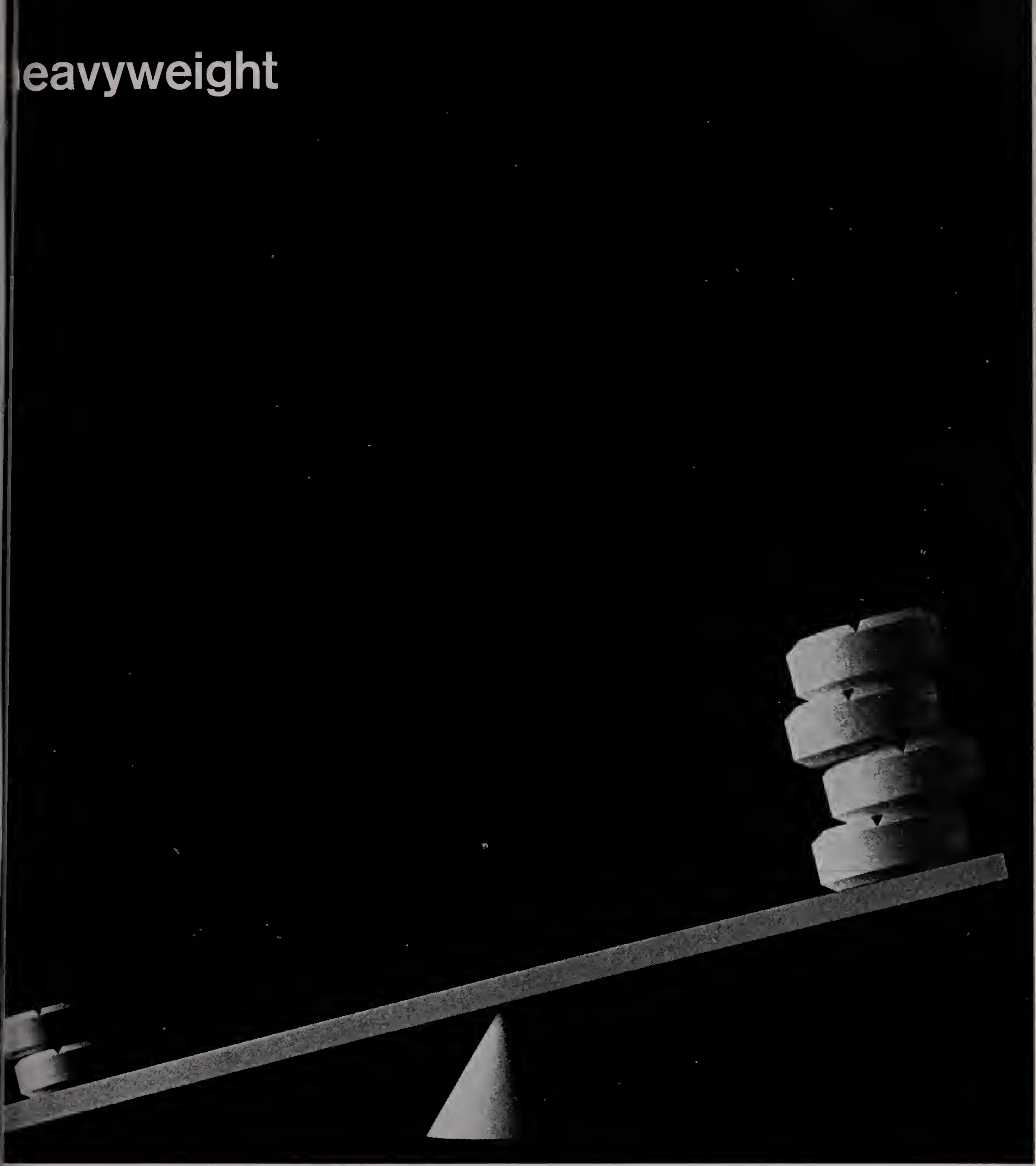

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(1) Frykman, H.M.: Minn. Med., Vol. 38, Jan. 1955. (2) Poth, E.J.: The J.A.M.A., Vol. 163, No. 15, April 13, 1957. (3) McGivney, J.: Texas State Jour. of Med., Vol. 51, No. 1, Jan. 1955. (4) Stern, F. H.: Jour. of The Amer. Ger. Soc., Vol. 11, No. 3, Mar. 1963. (5) Weekes, D. J.: N.Y. State Jour. of Med., Vol. 58, No. 16, Aug. 1958. (6) Abbott, P.L.: Jour. of Oral Surg., Anes. & Hosp. Dental Serv., Vol. 19, July 1961. (7) Weekes, D. J.: E.E.N.T. Digest, Vol. 25, No. 12, Dec. 1963.

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Number 6

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Ash hopper for leeching potassium from wood ashes, which was mixed with fat to make soap; reconstruction at New Salem, Illinois near Lincoln's home. W. D. Snively, Jr., M.D.; Mead Johnson Company, Evansville, Indiana

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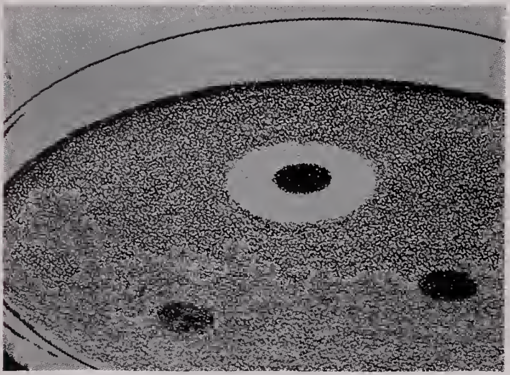

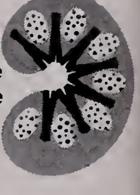

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References: (1) Carroll, G.: Urologists' Letter Club, June 1, 1964. (2) McDonald, D. F., and Short, H. B.: Address to the Fourth Interscience Conference on Antimicrobial Agents and Chemotherapy, New York, Oct. 26-28, 1964.

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Contraindicated in comatose or greatly depressed states due to CNS depressants and in cases of existing blood dyscrasias, bone marrow depression and pre-existing liver damage. *Principal side effects,* usually dose-related, may include mild skin reaction, dry mouth, insomnia, fatigue, drowsiness, dizziness and neuromuscular (extrapyramidal) reactions. Muscular weakness, anorexia, rash, lactation and blurred vision may also be observed. Blood dyscrasias and jaundice have been extremely rare. Use with caution in patients with impaired cardiovascular systems.

Before prescribing, see SK&F product Prescribing Information.

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President's Letter

There has just come across my desk a report of the First National Conference for Professional Nurses and Physicians, sponsored by the American Nursing Association and the American Medical Association. This conference, which was held in 1964, was devoted to major problems in the relationships of our two professions. There was much discussion about the independent and divergent paths which professional nursing has taken when appraised in the light of the traditional concept of the nurse as held by most physicians. If one conclusion may be cited, it was the need jointly to discuss, understand, and evaluate our separate roles in the good care of the patient.

In most hospitals today the physician encounters a rather formally organized nursing service. There is a graduate nurse who is a supervisor or leader of a group which may include graduates on floor duty, licensed practical nurses, nurses' aides, diploma or three-year students, and perhaps college degree students. Each is usually identified by a distinctive uniform, often in a pastel color, and each has or should have a well understood function in patient care, assigned according to training and ability. When there is a student program, direction most likely comes from an administration which is not primarily concerned with patient care but with the learning experience of the student, and in many student programs actual nursing service is minimal. This is hard for a physician to understand, and it is also an additional item in the cost to the patient if the cost of an educational program is included in the daily charge which the hospital makes. Lessened student hours of patient care and the shortened work week of graduate nurses have contributed to a shortage of personnel actually engaged in nursing care which is of vital concern to all.

In contrast to the organized nursing staff responsible to the hospital administration for the most efficient care possible, the physicians of the staff are often highly individualistic with many variable concepts of what should be done for their patients. It is understandable that conflicts of opinion should arise. Probably few of us would really be willing to turn back the clock. We realize that in our busy hospital practice the well educated graduate nurse of today, trained with the knowledge of medical science to understand the increasingly complex procedures of modern medicine and to direct a nursing group, is an essential part of the medical team. But the nursing profession and the hospital administration must not lose sight of the individual physician's intense concern for every facet of the patient's care. None of us, physician, nurse and administrator, should be too busy to find time to discuss and understand the others' problem and to plan cooperatively so that each knows the role of the other.

I will close this letter with one practical suggestion. When things go wrong do not castigate the first uniformed female you see but seek out the person in charge and find a quiet place to present your problems. If there are interns and residents they will profit by your example and your patients or the relatives in the hall will not become unduly alarmed or perhaps amused.

JMStickney M.D.

J. M. Stickney, M.D.
President
Minnesota State Medical Association

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The Clinician Views Potassium Deficit

W. D. SNIVELY, JR., M.D.*
R. L. WESTERMAN, M.D.**
Evansville, Indiana

THE ELECTROLYTE potassium has great clinical importance, yet contrasts and paradoxes lace its story. Although essential for life and deeply involved in that vital wellspring, the cell, potassium can be the deadliest of poisons. Resembling its close relative sodium in chemical nature, it strikingly opposes sodium in most of its physiologic actions. Although the body contrives to keep the cellular concentration of potassium at a high level — in defiance of known physical-chemical laws — it fails to conserve potassium, even when the patient is dying of a deficit.

As Fenn[1] pointed out, "A normal adult has enough potassium in his body to kill 100 people if it were injected into their blood, yet if he got no potassium in his diet he would soon be paralyzed and die." Should the concentration of plasma potassium increase to more than three or four times normal, the heart will stop beating. If as little as 6 per cent of cellular potassium could escape quickly into the extracellular fluid, one would quickly die. Although the usual human intake of potassium is about 3 grams (approximately 77 mEq.) a day, one could become gravely ill from the potassium ingested at a single meal if the kidneys and body cells did not keep watch over the rising level of plasma potassium derived from absorbed food.

Incidence of Potassium Deficit

The studies of Surawicz and others[14] revealed the high incidence of potassium deficit in many hospital patients. During the period from October 1, 1954, to April 30, 1955, they determined the plasma potassium level in 1,497 adult male and 1,289 adult female inpatients of the Philadelphia General Hospital. Potassium concentrations below 3.5 mEq./L were found in 273 men (18

TABLE I
Plasma Chemical Constituents: Normal Ranges[9]

Plasma Na^+	137-147 mEq./L
Plasma K^+	4.0-5.6 mEq./L
Plasma Ca^{++}	4.5-5.8 mEq./L
Plasma Cl^-	98-106 mEq./L
Plasma Protein	6-8 Gm./100 ml.
Plasma HCO_3^-	Adults: 25-29 mEq./L Children: 20-25 mEq./L
Plasma Cl^- plus Plasma HCO_3^-	123-135 mEq./L
Plasma pH	7.35-7.45
Plasma HPO_4^{--}	1.7-2.6 mEq./L

Urine Values

Urine pH	4.5-8.2
Urine specific gravity	1.010-1.030

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**Protestant Deaconess Hospital.

per cent) and in 284 women (22 per cent). Berger[34] used negative potassium balance and decreased plasma chloride with elevated bicarbonate as criteria for the diagnosis of potassium deficit, in surveying the entire patient population of a small general hospital. Twenty per cent (24 of 120) exhibited potassium deficit. In emphasizing the high incidence of potassium deficit, Berger[42] stated that it can occur in pediatric, medical, and surgical patients.

When Read and others[15] administered chlorothiazide to patients with ascites resulting from liver cirrhosis, they found an increase in the urinary output of potassium. All patients who did not receive potassium supplements developed hypokalemia.* Bartels and others[17] administered chlorothiazide to 65 patients with hypertension; 28 patients (43 per cent) showed a drop in potassium level to 3.5 mEq./L or below. Relman and Schwartz[11] emphasized the frequency of the nephropathy of potassium depletion.

Physiologic Considerations

As Nicholson and Herring[6] pointed out, potassium should be viewed as an element that exists in the fluids of the body in concentrations that are reasonably constant for each body fluid. Of the adult's 3,000 mEq. of potassium, only 50 to 70 mEq. are normally contained in the extracellular fluid.

The exact minimal daily requirement for man is not known. On a normal, average diet, deficiency of potassium does not occur since this element is found in practically all foodstuffs. Dietary intakes of potassium in normal adults have been found to range from a low of 51 mEq. to a high of 125 mEq. per 24 hours. Normally, about 80 to 90 per cent of ingested potassium is excreted in the urine, with the remainder in the stools and sweat. Fasting adults without any sodium intake soon compensate and excrete little sodium after the second day of such a fast. In contrast, if an adult is fasting or on a diet adequate in calories but potassium free, urinary loss of potassium continues in the amount of 40 to 50 mEq. daily. The daily loss is even more important in children, who have a greater potassium exchange than adults.[29]

Luetscher and Curtis[8] early emphasized the importance of aldosterone in the regulation of sodium and potassium balance. One mechanism for the conservation of sodium involves the production of additional aldosterone. While conserving sodium and water, aldosterone increases the excretion of potassium. In addition to the aldosterone mechanism for potassium excretion, there is another kidney mechanism that helps regulate potassium: the distal convoluted tubules of the kidney secrete potassium into the urine whenever the potassium concentration becomes too high in the extracellular fluid. This effect presumably is brought about by the direct stimulation of high potassium concentration on the tubular epithelial cells.[38]

Excretion of potassium via the urine follows a fairly fixed pattern.[37,40] The diurnal rhythms of excretion of potassium, sodium, and chloride appear to be under the control of subcortical parts of the brain, such as the hypothalamus.[51]

While the consensus appears to be that conservation of potassium is almost nonexistent, Berman[43] maintained that potassium conservation does occur, at least to a limited extent.

Etiology

Cannon[7] emphasized that potassium deficit may be found in a great variety of clinical conditions. We have summarized the usual antecedents of potassium deficit as follows:

I. *Conditions Causing Excessive Loss of Potassium from the Body*
A. Medical Therapy
thiazide-type diuretics[15-19,31-33,41,53]
adrenal steroids
infusion of solutions of saline or dextrose not containing potassium
treatment of diabetic acidosis
excessive laxation[6,20]
repeated enemas[10]
mercurial diuretics, alone or with ammonium chloride
ion exchange resins
therapeutic low sodium diet
absorption of fludrocortisone[24]
disulfiram alcohol reaction
administration of radioactive iodine

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*See Test Your Word Score Page 763.

- B. Surgical Therapy
  - ileostomy
  - colostomy
  - ureterosigmoidostomy[22]
  - resection of large portion of large or small intestines
  - gastric or intestinal tubal drainage
- C. Metabolic Diseases
  - periodic familial paralysis
  - excessive production of aldosterone, as in nephrosis, cirrhosis, or malignant hypertension
  - stress syndrome (whether physical, as in chronic illness, or psychological, as in severe emotional depression)
  - diabetes insipidus
  - uncontrolled diabetes mellitus
  - aminoaciduria
  - alkalosis
  - Cushing's syndrome
  - massive breakdown of body protein
- D. Diseases of the Intestinal Tract
  - ulcerative colitis
  - diarrhea, with or without vomiting
  - fistula of the small or large intestine
- E. Trauma
  - massive destruction of tissue
  - severe burns
  - wound exudation
  - crush syndrome
- F. Renal Disease
  - chronic nephritis
  - diuretic phase of nephritis

II. *Conditions Involving Increased Utilization of Potassium by the Body*
  - healing phase of burns
  - recovery from diabetic acidosis

III. *Conditions Characterized by Decreased Intake of Potassium*
  - poor nutrition[5,23]
  - nausea
  - anorexia[27]
  - acute alcoholism
  - starvation of disease
  - therapeutic starvation

Sackner and others[31] emphasized that claims that one benzothiadiazine compound causes less potassium depletion than others are meaningless unless endogenous aldosterone secretion, which of itself causes potassium excretion, is considered. Relman[39] emphasized that primary aldosteronism causes recurrent or persistent hypokalemia. Thus the finding of unexplained hypokalemia should alert the clinician to the possibility of primary aldosteronism.

Symptoms and Physical Findings

Probably the most common symptom of potassium deficit is malaise, often expressed as "just not feeling well." Since potassium deficit may be associated with other illnesses, this symptom may not impress either the patient or the physician. Muscular weakness is almost always noted and should lead one to suspect potassium deficit. In chronic potassium deficit, malaise and muscular weakness may persist for many months and be interpreted as being due to emotional instability, neurasthenia, or psychasthenia. Berger[42] has characterized the clinical features as follows:

1. *neuromuscular features,* including weakness, diminished to absent reflexes, confusion, muscles flabby like a half-filled water bottle. The patient lies flat like a cadaver, not rounded.
2. *cardiovascular features,* including weak pulse and faint heart sounds. Later, heart block and falling blood pressure may appear.
3. *gastrointestinal features,* including vomiting and paralytic ileus.
4. *respiratory features,* including shallow respiration.

Nicholson and Herring[6] have emphasized the need for care in distinguishing between hypokalemia and hyperkalemia. Holliday and others[28] emphasized that polydipsia occurs frequently in potassium deficit. Weisberg[29] stated that specific clinical manifestations of themselves are of little help in the early recognition of body potassium deficit.

Pathologic Lesions

When Darrow[12] first described clinical potassium deficit in infantile diarrhea, he was focusing interest on an ailment that had been almost universally fatal. Little or no interest was expressed in the after-effects of potassium deficit. Perkins and others[2] in 1950 focused attention on the possible sequelae of prolonged potassium deficit when they reported the necropsy of a patient with chronic diarrhea, who had shown clinical, laboratory, and electrocardiographic evidence of potassium deficit. The following lesions were found:

Focal myocardial necrosis with cellular infiltration and fibrosis

Focal endocarditis

Pronounced hydropic degeneration of the renal tubules

These lesions, identical to those reported in potassium-deficient animals, have been repeatedly observed after chronic potassium deprivation.[3,4,11,21,22,23,27,28,35,36,42,44]

Newberne[44] found that prolonged potassium deficit causes severe damage in the heart and kidneys of the rat. The pathologic alterations observed in the heart indicate that the primary site of injury is the myocardial fiber. The kidney cortex had dilated tubules, some containing casts. Most of the tubules at the corticomedullary zone and outer medulla were grossly dilated.

Diagnosis

Determination of the plasma potassium can be helpful in diagnosis of potassium deficit if its limitations are understood and if repeated determinations are made. Simultaneous determination of the concentrations of sodium, chloride, and bicarbonate, as well as the packed cell volume, add valuable information useful when aggressive electrolyte repair is planned. The electrocardiograph can help, although in the presence of severe myocardial damage following infarction or digitalis intoxication, the typical picture of potassium deficit may be obscured.

Darrow[12] and, later, Snively and Sweeney[9] placed great emphasis on the usefulness of the clinical history in diagnosing potassium deficit. While Weaver and Burchell[25] maintained that a definite correlation can be established between the electrocardiogram and the serum potassium level at hypokalemic values, a normal electrocardiogram does not exclude hypokalemia. An electrocardiogram fulfilling the usually established criteria for hypokalemia is not pathognomonic of the condition.

Sweeney's[30] simple, yet comprehensive method of diagramming electrolyte deficits and excesses places due emphasis on the partition of potassium and other electrolytes between the cells and the extracellular fluid.

The normal concentrations of potassium within the plasma makes minor variations important.[32] As Berger[34] stated, one requires repeated determinations of the plasma potassium level to diagnose potassium deficit. Urinary excretion of more than 70 mEq. of potassium per 24 hours when the patient is on a normal diet should suggest excessive loss of potassium. An increasing plasma bicarbonate plus a decreasing plasma chloride indicate a developing potassium deficit. In alkalosis, chloride is lost, probably because the potassium in the extracellular fluid is excreted rapidly as potassium chloride. The hypochloremia results in loss of an anion, which can be met only by an increase in the readily available bicarbonate.

As Moyer[19] pointed out, the symptoms of opposed imbalances may neutralize each other. However, such composite pictures are of more theoretical than practical interest.

Laboratory tests especially helpful in the diagnosis of body potassium deficit include the urine pH, urine potassium, plasma potassium, plasma chloride, plasma bicarbonate, and plasma pH. Usually, in a well-de-

TABLE 2

Plasma Chemical Constituents: Average Values in Health[9]

Plasma Na^+	142 mEq./L
Plasma K^+	5 mEq./L
Plasma Ca^{++}	5 mEq./L
Plasma Cl^-	103 mEq./L
Plasma Protein	7.0 Gm./100 ml. (16 mEq./L)
Plasma HCO_3^-	Adults: 27 mEq./L Children: 23 mEq./L
Plasma pH	7.4
Plasma HPO_4^{-}	2 mEq./L
Urine Values	
Urine pH	6.0
Urine specific gravity	1.015

TABLE 3

Useful Potassium Information

To convert milligrams/potassium to milliequivalents/potassium, multiply milligrams by .0256; thus, 100 mg. potassium equal 2.56 mEq.

Remember:

1. If pH of extracellular fluid decreases, extracellular potassium rises; if pH of extracellular fluid rises, extracellular potassium decreases.
2. If dextrose enters the cells, plasma potassium also enters the cells; the plasma potassium level decreases.
3. Potassium and hydrogen compete for excretion but exchange with sodium in the distal convoluted tubule. Therefore, if plasma potassium goes down, hydrogen may be excreted preferentially.
4. Aldosterone favors conservation of sodium — excretion of potassium.
5. Potassium is primarily cellular; 98 per cent of the body's potassium is within the cells.
6. The plasma potassium level at a given moment is the end product of a variety of factors — only one of which is the body's potassium stores.

veloped deficit of potassium, the urine pH will be alkaline; the urine potassium will be increased over 70 mEq. every 24 hours; the plasma potassium will be decreased; the plasma chloride will be decreased; the plasma bicarbonate will be increased; and the plasma pH will be increased. Information of interest in diagnosis of potassium deficit is presented in Table 3.

Management

Prevention

The physician can frequently anticipate potassium deficit by awareness of the predisposing clinical conditions. Correction of such conditions — for example, diarrhea — stops the potassium loss and makes unnecessary the preventive administration of potassium.

Potassium deficit can be prevented by including adequate potassium in parenteral infusions of electrolytes and dextrose; by avoiding the persistent use of laxatives or enemas; by the prompt correction of vomiting; by the replacement of electrolytes lost through fistulas of the small intestine or colon; by prompt diagnosis and correction of aldosterone-producing tumors of the adrenal cortex; by replacement of electrolytes lost through ileostomy or colostomy or ureterosigmoidostomy; by the careful observation of the patient undergoing severe physical or emotional stress; by the prompt diagnosis and treatment of diabetes insipidus or diabetes mellitus; by the prompt correction of renal disease in which excessive potassium is being lost in the urine; by meticulous attention to the nutrition of sick persons such as those with prolonged nausea, chronic infectious disease, anorexia nervosa, or alcoholism.

In considering administration of potassium for prevention of potassium deficit, one should recall that normally about 80 per cent of the potassium ingested is excreted in the urine, the remainder being excreted in the stools and perspiration. Fasting adults on a diet adequate in calories but potassium-free, lose from 40 to 50 mEq. of potassium each day in the urine. Martz[36] has emphasized the need for administering supplementary potassium for patients receiving thiazide diuretics.

The oral route is the best route for prophylactic administration of potassium. If oral administration is impossible, then administration by nasogastric tube or by rectal infusion should be considered. Potassium can be administered prophylactically either through the use of foods high in potassium or through potassium-containing mineral supplements. In order to obtain the potassium required by ingestion of high-potassium foods, the patient is forced to eat relatively large quantities of these foods, which he may not like, or which may not be readily available. Potassium supplements, on the other hand, are readily available. Various potassium-rich foods are listed in Table 4.

TABLE 4
Potassium Content of Potassium-Rich Foods

	Potassium-Milli-equivalents
Fruits	
Apricots, raw, 2-3 medium	7.06
Banana, 1 medium	16.12
Dates, dried, 3-4	5.78
Figs, raw, fresh, 2 large	4.86
canned in syrup, 3 figs, 2 Tbsp. syrup	2.68
dried, 7 small	19.96
Oranges, 1 medium 3", size 200	9.21
Peaches, dried, ½ cup, uncooked	28.16
Prunes, dried, raw, 5 large	7.68
Raisins, dried, seedless, 2 Tbsp.	3.68
Juices	
Tomato, ½ cup, canned	7.29
Orange, ½ cup, fresh	5.68
Miscellaneous	
Bre'r Rabbit Syrup, 1 Tbsp.	6.91
5 Tbsp.	34.56
Brazil Nuts, shelled, 4 medium	2.56
shelled, 1/3 cup	17.15
Instant Coffee, Folgers, 2 gm. dry in 240 cc. water	6.14

For years potassium chloride has been regarded as a satisfactory source of oral potassium, despite the fact that it is relatively irritating to the gastric and intestinal mucosa. Now, serious questions have been raised as to the safety of potassium chloride. Lindhomer[46] reported 20 patients with stenosis and ulcer of the small intestine, which apparently resulted from the ingestion of enteric-coated potassium chloride. Baker and others[49] reported primary nonspecific ulceration and stenosis of the small intestine in 12 patients in one hospital over a 15-month period. Eleven were receiving enteric-coated potassium chloride at the time of the acute illness. In an editorial in the same issue of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION,[50] the validity of the findings of Baker and others was corroborated. Use of potassium salts other than the chloride, and especially other than the enteric-coated chloride, appears desirable for prophylaxis. Recent corroboration of the potential hazards of enteric-coated potassium chloride includes articles by Buchan and Houston,[54] Morgenstern and others,[55] and Lawrason and others.[56]

The usual dose for prophylaxis of potassium deficit is 50 mEq. daily, in addition to that contained in a well-balanced diet. A useful rule of thumb suggests that the patient receive a daily quota of potassium equal to his daily urinary excretion plus 10 per cent. Thus, if a patient was found to be excreting 160 mEq. of potassium in the urine each day, the correct total potassium intake for prevention of a deficit would be 176 mEq. daily. If the dietary intake of potassium was estimated at 75 mEq. then one would administer about 100 mEq. of potassium as a supplement.

Correction

Correction of potassium deficit should be carried out by the oral or nasogastric route, if possible.[6,9,13,42] Workers have agreed that potassium, as well as other electrolytes, should not be given parenterally except by the intravenous route, since subcutaneous and intramuscular injection of water and electrolytes present many unjustifiable hazards.[9]

Flear and others,[13] and De Graeff and others[52] emphasized the association of potassium deficit with alkalosis. If the ingestion of chloride in the diet is not sufficient to produce a normal plasma chloride, then ammonium chloride should be given along with the chloride-free potassium salt. Measurements of the plasma chloride and bicarbonate, as well as the potassium, can help the physician determine whether it is necessary to give ammonium chloride or not.

Winsor[26] stated that the use of potassium salts in the treatment of digitalis toxicity should be undertaken with caution, while emphasizing that digitalis intoxication can appear for the first time when hypokalemia develops and that the correction of hypokalemia may decrease the signs and symptoms of digitalis intoxication.

Any treatment regimen for potassium should include not only correction of the deficit, but administration of amounts adequate for daily maintenance. If the patient has been vomiting, one should replace such amounts of potassium and chloride as are lost in the vomitus. Should any question exist as to the safety of administration of potassium, the physician can proceed as long as repeated plasma levels are normal. If the level is not rising or if the individual has normal renal function and is excreting about 2 ml. of urine per minute (120 ml. of urine per hour), the chances of producing potassium accumulation are so small as to be negligible.

The possible value of administration of potassium to restore myocardial response to a failing cardiac pacemaker has been discussed pro and con in the recent literature.[47,48]

Summary

Deficit of potassium is a more prevalent clinical condition than commonly appreciated. It depends in part on the body's strange failure to conserve potassium efficiently. It can be caused by excessive loss of potassium from the body, increased utilization, or decreased intake. Early, the symptoms and physical findings of potassium deficit are vague and confusing. Later, they become all too clear, and include widespread weakness of intestinal, cardiac, and skeletal muscle. Pathologic changes in the heart and kidneys have been observed following prolonged potassium deficit. Diagnosis of potassium deficit is based on the clinical history, symptoms, and physical findings. A systematic and comprehensive analysis of the recent history is required, particularly for early diagnosis. The physician can frequently anticipate potassium deficit by a thorough knowledge of how potassium deficits develop. In many clinical states, administration of supplementary potassium will be needed if one is to prevent the accumulation of a deficit. Management of potassium deficit calls for the administration of potassium, preferably by the oral route. Oral administration of potassium is best carried out by the use of a chloride-free salt of potassium. If additional chloride is required because of the presence of a chloride deficit (as in hypokalemic alkalosis) chloride can be administered via dietary sources or as a salt of chloride.

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21-56 May be obtained from the author or the reprints.

The Penalty of Overweight

Obesity alone can be the cause of pathologic changes in the heart and of heart failure. — MacBryde, M.D., Signs & Symptoms, Lippincott Co.

If the God of goodness and indulgence who hovers over the world does not make a second washing of the human race, it is doubtless because so little success attended the first. — Balzac

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The world is full of willing people; some willing to work, the rest willing to let them. — Robert Frost

Pyelographic Changes

in Decreased Renal Blood Supply*

THE PYELOGRAPHIC changes associated with a decrease in the renal blood supply can be placed in essentially five different categories: 1. Difference in renal size; 2. Normal or no detectable change on routine examination; 3. Difference in opacification in the nephrographic phase or in the pyelographic phase; 4. Nonfunction; 5. Pyelonephritis.

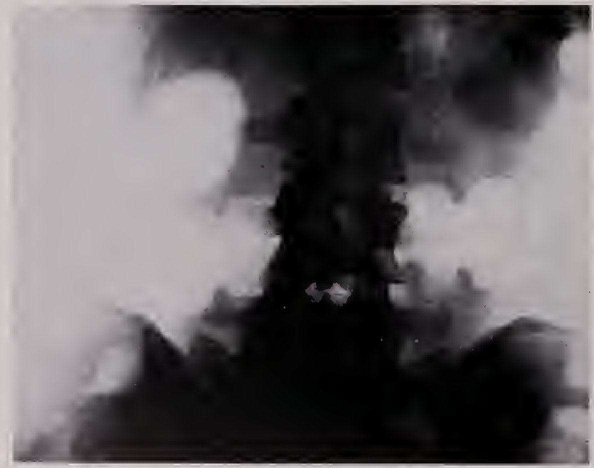

Fig. 1 — Reduced immediate nephrographic effect on the right in a 19-year-old girl with hypertension.

Illustrative Cases

Disparity in the Nephrographic Phase of Excretion

Figure 1 is a film exposed for 30 seconds after injection of routine contrast material in a 19-year-old girl with diastolic hypertension. There was an excellent nephrogram on the left but reduced immediate nephrographic effect on the right.

Disparity in Density at the Pyelographic Phase, Difference in Renal Size, and Pyelonephritis

Figure 2 represents a film taken 26 minutes after injection of the contrast material in the same individual as illustrated in Figure 1. This shows a good concentration of contrast in a normal-size left kidney and reduced concentration in a smaller right kidney, plus changes associated with pyelonephritis. The right kidney was removed and her blood pressure returned to normal.

These four findings which can be isolated findings in individual cases were all demonstrable in this instance.

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*Read before the Minnesota Radiological Society Meeting, February 29, 1964, Minneapolis, Minnesota.

H. HARRISON EELKEMA, M.D.
St. Paul, Minnesota

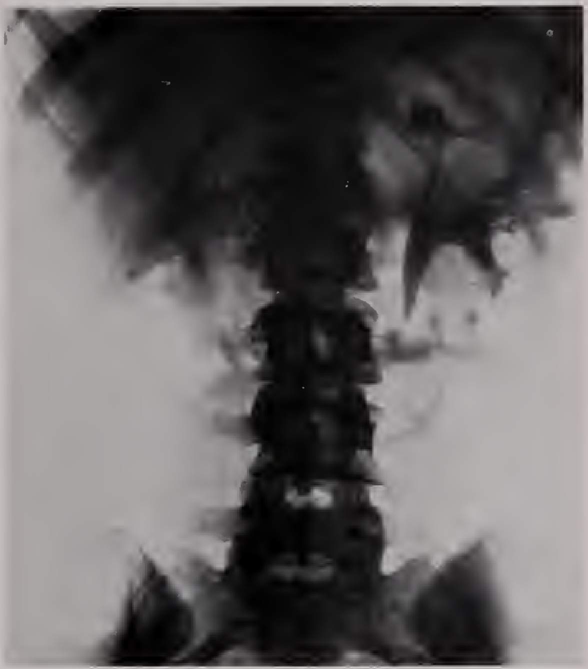

Fig. 2 — Same case as Fig. 1. Film at 26 minutes showing reduced concentration of contrast and smaller right kidney.

Complete Obstruction of the Left Renal Artery

Figure 3 illustrates nonfunction of the left kidney in a 71-year-old man whose presenting complaints were myocardial infarction and high blood pressure. Five months prior to this admission he had had pain in his left flank, followed by three days of bowel trouble. Retrograde examination revealed a normal collecting system, but the angiogram demonstrated complete obstruction of the left renal artery. The left kidney was removed and his blood pressure promptly returned to normal levels and has remained normal.

Stenotic Lesion of the Left Renal Artery

Figure 4 illustrates a normal urogram obtained in a 31-year-old man with diastolic hypertension, heart failure, and marked edema. It was subsequently demonstrated that he had a stenotic lesion in the left renal artery. Left nephrectomy was done when arterial reconstruction failed.

The above cases were selected for illustration from a group of 55 available for review. In over 50 per cent, abnormal findings such as nonfunction, marked variation in size, or excretion, were readily recognized and reported.

Difference in Contrast Density

In 11 cases the urogram was read as normal. These 11 cases were reviewed and classified as to positive or negative on the basis of (1) a difference in density in contrast, and (2) renal size (including circumferential measurements).

Differentiation by Difference in Density

In these 11 cases, differentiation by difference in densities was difficult. Aside from the difficulties in examination itself, such as preparation, state of hydration, technical factors, and presence of complicating medical conditions such as diabetes or heart failure, several other factors can be mentioned. The kidneys are richly supplied with blood and have been likened to an arterial venous fistula as far as oxygen consumption is concerned.

Figure 5 represents diagramatically a 70-kilogram man who has 5 kilos of blood, 7 per cent of his body weight. The middle fig-

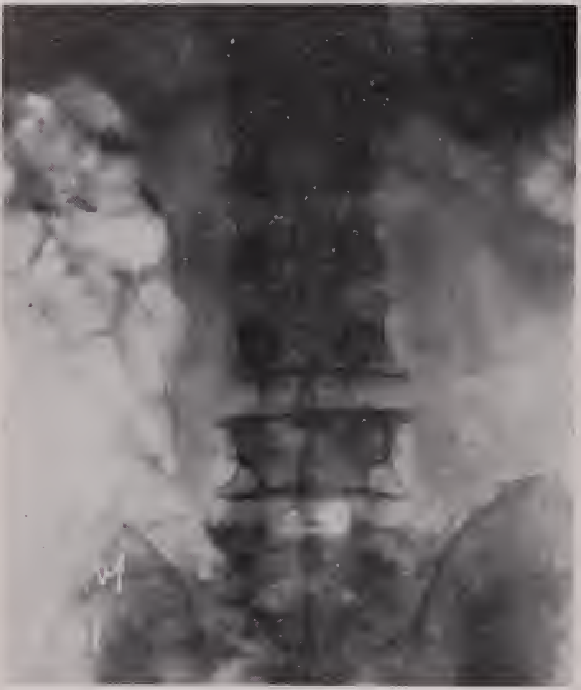

Fig. 3 — Nonfunctioning left kidney in a 71-year-old man subsequently proven to have left renal artery obstruction.

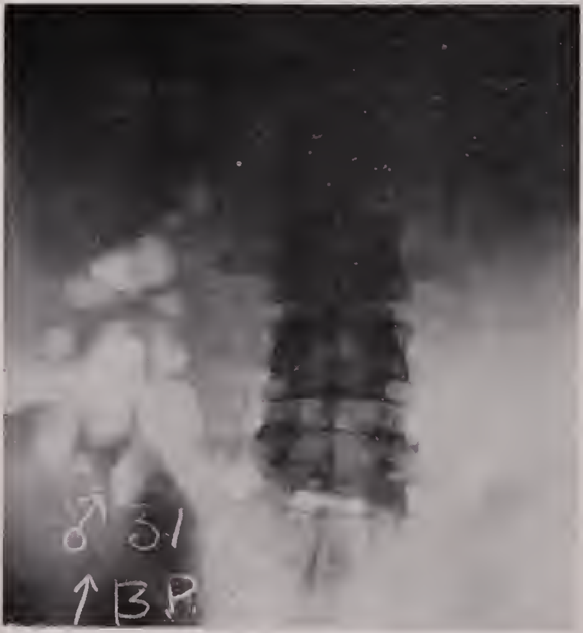

Fig. 4 — Examination considered normal in a 31-year-old man with clinically significant arterial obstruction on the left.

ure represents the renal mass of .3 kilos, 20 per cent of which is blood. The figure on the right represents the resting cardiac output, of which 20 per cent, or 1 liter per minute, profuses the kidneys. Very roughly, this would mean that in the resting phase the blood in the kidneys is changing fifteen times per minute. Even if blood flow to one kidney were reduced 30 to 50 per cent, there would still be a tremendous change of blood per minute through this organ.

Then consider that with contrast media now available we are offering the kidneys 10 grams of iodine, far in excess of what is necessary to do an adequate examination in a well prepared patient. The variability of water absorption with occlusive lesions of the renal artery also adds to the difficulty in evaluation of contrast density. Taking these into account, there appear to be adequate reasons for difficulties in appreciating slight differences in concentration of contrast.

Renal Size

Returning to Figure 5 note that approximately 20 per cent of the weight of the renal mass is blood. There is evidence beginning to appear in the literature that the change we see in length and size of the kidneys is not necessarily an atrophy of the kidney, but a change in the volume of blood and solute that is in the kidney at the time of examination. De Bakey has observed a revascularized kidney even at operation to increase in size. Drs. Kincaid and Utz, in Emmett's book, report that under general anesthesia the larger kidney which is being normally profused will decrease in size and approach the size of the affected kidney. With this in mind the 11 cases were reviewed and measurements in height, width, and circumference of the kidneys were obtained.

To acquire some idea of normal difference in length and circumference, 50 normal cases were reviewed. Measurements were made on films exposed 30 seconds after injection of contrast in which the renal outlines were brightened by the nephrographic effect. Circumferences were obtained by using a map measure. Figure 6 represents the results in these 50 normal tensive patients. Note that in 16 per cent of the cases there was a difference in length of 1 cm. or more. Only 6 per cent showed a circumference difference of 2 cm. or more. Figure 7 represents findings in the 11 "normal" urograms. Using length difference of 1 cm. or more 4 of 11 affected kidneys could be suspected. Using circumference difference of 2 cm. or more the side of the arterial lesion was indicated in 9 of 11 cases.

Discussion

In well over half of a series of 55 cases of renal vascular occlusion, routine pyelographic examination was useful as a screening procedure because of readily appreciated changes: namely, nonfunction, marked disparity in renal size and/or function, and unilateral pyelonephritis. In 11 patients with borderline or normal urograms, differences in density of contrast at the pyelographic phase were difficult to appreciate. Differences in renal size as a reflection of volume of blood and solute in the kidney may be a better point of differentiation. In this small series a difference in circumference greater than 2 cm. seemed to provide a more sensitive scale of separation than either observation alone, measurement of length, or evaluation of contrast density. A film exposed 30 seconds after contrast injection facilitates measurement because of the nephrographic effect.

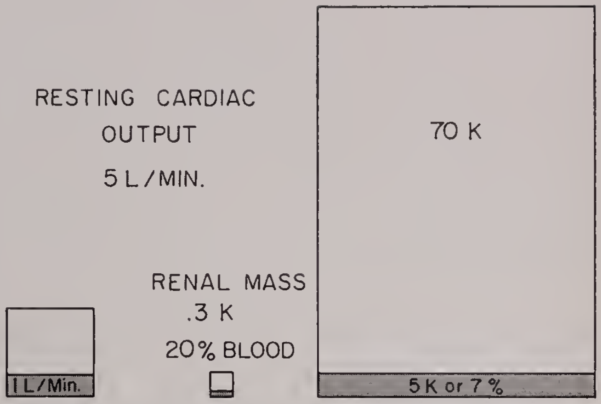

Fig. 5 — Diagram illustrating: 1. renal mass relative to body mass, 2. renal blood flow relative to resting cardiac output and 3. contribution of blood mass to total renal mass.

MEASUREMENTS IN 50
"NORMAL"
Averages

	R	L
Length	12.6	13.0
Width	5.8	6.1
Circ.	31.1	31.3
L. Diff.		16% Over 1 Cm.
Circ. Diff.		Only 6% Over 2 Cm.

Fig. 6

MEASUREMENTS IN 11
WITH UNILATERAL VASCULAR OBSTRUCTIONS
Averages

	R	L
Length	13.2	13.4
Width	5.7	6.0
Circ.	32.5	32.2
L. Diff.		4/11 Over 1 Cm.
Circ. Diff.		9/11 Over 2 Cm.

Fig. 7

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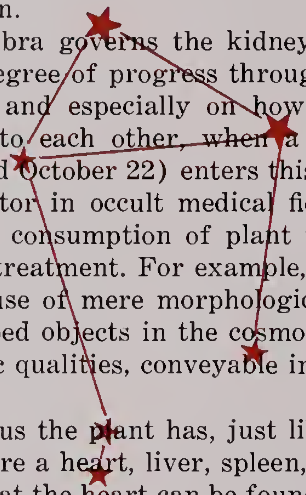
Drive Safely

One headlight is enough if the other driver guesses correctly which side it is on. — Herbert Prochnow

It is not evil that shocks, it is the unexpected. — Robert Penn Warren

Astrology and Medicine — Libra, the Balance

Libra, seventh sign of the zodiac, is represented by a pair of scales, denoting the ideal balance between the spiritual and material forces throughout the cosmos. The sun enters Libra about September 22, the time of the autumnal equinox, to remain there for one zodiacal month before entering Scorpio. On June evenings the constellation of the Balance is clearly visible and easy to identify, as it consists mainly of only two bright stars: alpha Librae, approximately on the ecliptic, and beta Librae, a little above and eastward of its companion.



In Astrology's book Libra governs the kidneys - for better or worse, depending on the sun's degree of progress through the sign; on the lunar and planetary positions, and especially on how the celestial bodies are aspected with reference to each other, when a Libra native (one born between September 22 and October 22) enters this world.

As pioneer and innovator in occult medical fields and in astrotherapy Paracelsus advocated the consumption of plant products shaped like the human organs requiring treatment. For example, kidney beans for kidney diseases! Not alone because of mere morphological similarity, but rather because all similarly shaped objects in the cosmos were thought to be imbued with similar esoteric qualities, conveyable in essence from one entity to another.

"According to Paracelsus the plant has, just like man and animal, in it his organs. In the herbs are a heart, liver, spleen, etc. just as in man. This does not mean, he says, that the heart can be found in the plant as it can by man, but that it is present as a power and a virtue, like to the heart. In the first place Paracelsus seeks the conformable shape in the plants, - conformable to man and Cosmos, and he usually administered the plant which in shape conformed to the sick organ or part of the body, because according to his theorem both the sick organ and the agreeing plant took their shape from the same principle in the Cosmos; it therefore might be expected that the healthy principle in the plant would come to the aid of the sick principle of the part of the body."*

Preposterous? Maybe! But wasn't it Hamlet who said: "There are more things in heaven and earth, Horatio, than are dreamt of in our philosophy."

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*C. Aq. Libra: Astrology, Its Technics and Ethics. P. Dz. Veen, Amersfoort The Netherlands, 1917, p. 207-208.

Pinch the Baby Before Landing

Robert L. Wick, M.D. has observed that middle ear trouble can occur when the plane lands and he recommends that in order to prevent the baby from having ear block the very small child should be pinched and made to cry for a very few minutes while coming down, as this would be preferable to hours of crying on the ground until the ear block can be relieved.

— Medical Times, March, 1965.

That indolent, but agreeable condition of doing nothing. — Pliny the Younger

Diabetes Detection

Use of A Mobile Diabetes Detection Laboratory

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THE EARLY discovery of currently undiagnosed cases of diabetes mellitus in the United States constitutes a real challenge to the medical profession, the public health services, and our entire society. The magnitude of the problem is reflected, at least in part, by the prevalence rate of this disease.

Incidence of Diabetes

In 1946 studies in Oxford, Massachusetts, revealed that 1.7% of the population had diabetes, with only 50% aware of the diagnosis.[1] On this basis it was estimated that there were approximately one million undiagnosed cases of diabetes in the United States at that time.

More recent surveys have revealed that by 1962 there were two million persons in the United States, or 1.8% of the population, with *known* diabetes.[2] The prevalence of the undetected cases still remains uncertain but is generally agreed to equal at least the number of known cases. On the basis of the U. S. Public Health Service survey from 1959 to 1962, there are more than four million persons, aged 18 to 79 years, in the United States who have a "true blood glucose" of 200 mg.% or higher, one hour after a challenge dose of 50 grams of oral glucose.[2] This estimate specifically excludes persons with known or questionable diabetes. Admittedly, not all of these persons with evidence of impaired glucose tolerance would prove by more rigid criteria to actually have diabetes mellitus. However, the probability of diabetes in this group must be considered quite high.

The striking incidence of this disease is only one factor indicating the need for newer and broader programs of case finding. Social, economic, and medical factors are equally compelling; the total benefits resulting from early diagnosis are immeasurable both for the community and for the pa-

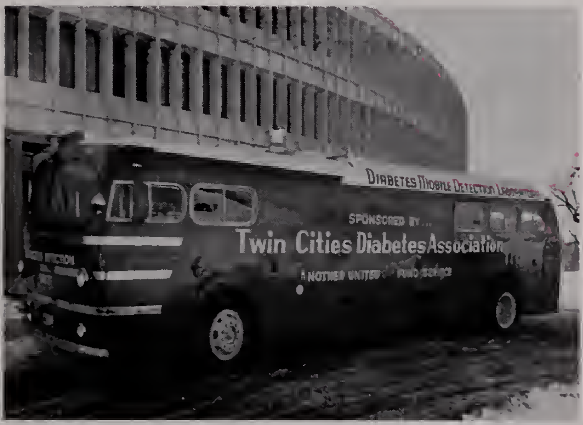
DIABETES MOBILE DETECTION LABORATORY
SPONSORED BY...
Twin Cities Diabetes Association
ANOTHER UNITED FUND SERVICE

Fig. 1 — Exterior view of Mobile Diabetes Detection Laboratory

tient. Prompt recognition of the disease can be expected to prevent most of the explosive symptoms. Some of the complications and associated manifestations can possibly be prevented or at least delayed in onset. In certain select individuals the early application of treatment may result in improvement of the decreased carbohydrate tolerance.

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Method of Detection

Until recently most screening programs for diabetes have utilized urine-testing methods; however, there are certain disadvantages to urine tests for mass diabetes detection.

Urine vs. Blood

Our experience from 1959 to 1961 revealed that only 15% of the distributed urine-test kits were utilized and returned for processing.[3] Urine tests also provide a rather low relative sensitivity as compared to blood tests for diabetes detection.[4] Screening procedures for diabetes using blood specimens and the Clinitron have been previously described by Parker et al.[5] This report will briefly present our experience with the Clinitron in a mobile laboratory unit.

Mobile Laboratory

In 1963 the Twin Cities Diabetes Association put into operation a Diabetes Mobile Laboratory (Fig. 1). This unit was designed to meet the complete needs for patient registration, public education, and laboratory functions (Fig. 2). Special considerations were given to providing a complete power generator, adequate internal water supply, air conditioning, and heating units. Provisions were made to utilize local water and power supply whenever readily available. The laboratory section was equipped with the Hewson Clinitron using the Wilkerson-Heftman method for blood sugar determinations.[6] The ruggedness of the instrument and its relative simplicity of operation made it highly adaptable to the mobile laboratory.

Disposable Equipment

Special emphasis was placed on utilizing disposable equipment to a maximum. Sterile disposable lancets were used to obtain fingertip blood specimens. A highly accurate disposable micropipette was developed with the co-operation of Dade Reagents, Inc.* The pipettes are 12.5 cm. in length and constructed of nonsiliconized tubing calibrated to 0.10 ml. and 0.1125 ml. Detailed information for operation of the Clinitron can be found elsewhere in the literature.[7] A screening level of 130 mg.% was employed for all tests. Patients with known diabetes were excluded. Persons with a "positive" screening test were retested with a modified oral glucose tolerance test. This procedure consisted of obtaining fasting and two-hour blood specimens after a challenging dose of 100 grams of glucose. True blood glucose determinations were employed for the tol-

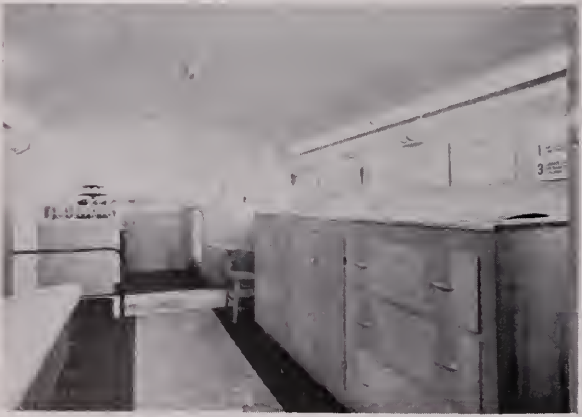

Fig. 2 — Interior view of Mobile Diabetes Detection Laboratory

TABLE 1
Mobile Diabetes Detection Laboratory, 1963 Results of Diabetic Screening Using the Hewson Clinitron

Total number of persons tested	6,627	
Test failure or breakage	22	
Net satisfactory results	6,605	(100 %)
"Negative" test at 130 mgs.%	6,431	(97.4%)
"Positive" test at 130 mgs.%	174	(2.6%)

TABLE 2
Mobile Diabetes Detection Laboratory, 1963 Results of Modified Oral Glucose Tolerance Test in "Positive" Reactors

Number of "positive" screening tests	174	
Number tested with oral G.T.T.	84	
Abnormal tolerance test	50	(59.5%)
Borderline tolerance test	7	(8.3%)
Normal tolerance test	27	(32.2%)

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*Dade Reagents, Inc., Miami, Florida.

TABLE 3
Mobile Diabetes Detection Laboratory, 1963 Relationship of Food Intake to Results of Screening Test and Tolerance Tests

Time of Food Intake in 84 Persons	Number Positive	Modified Glucose Tolerance Test Abnormal	Borderline	Normal
Less than one hour	15	4	1	10
1 to 2 hours	36	23	2	11
		(67%)		
2 to 3 hours	24	17	2	5
3 to 4 hours	7	5	1	1
More than 4 hours	2	1	1	0

erance test. Values below 110 mg.% at these times were considered *normal* and values above 130 mg.% were considered *abnormal* for purposes of this study. Values of 110 to 130 mg.% were considered as *borderline.*

Results

For about six months during 1963 a total of 6,627 patients were tested (Table 1). The bulk of the persons screened were middle-aged asymptomatic employees of a few selected companies and persons visiting large shopping centers. Of the 6,605 satisfactory tests 174 or 2.6% had a "positive" screening result. The results of retesting with the modified oral glucose tolerance test are summarized in Table 2. Slightly less than one half (48.2%) of the "positive" reactors returned for the tolerance testing. In the 84 persons who were retested, 59.5% were distinctly *abnormal* and 8.3% were *borderline* in their response to a challenge dose of oral glucose. These results indicate a probable incidence of previously *unknown* diabetes mellitus in at least 1.5% of the tested population.

In the persons with a "positive" screening test one to three hours after food intake, 67% also had an abnormal oral glucose tolerance test (Table 3). Although the numbers are small, persons with a "positive" screening test within one hour of food intake are most apt to have a *normal* tolerance test.

Summary

1. Retesting of "positive" reactors with an oral glucose tolerance test revealed an incidence of 1.5% of previously undiagnosed diabetes mellitus in a small population sample.
2. Initial screening with the Hewson Clinitron at a value of 130 mg.% should be done one to three hours after ingestion of food in order to achieve a high degree of specificity.

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The Tobacco Tyrant

There's at least one bright note for smokers. The evidence linking cigaret smoking to athlete's foot is statistically inconclusive. — Changing Times

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Life is too short to be small. — Disraeli

Rudimentary Uterine Horn Pregnancy*

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THE DIAGNOSIS of a ruptured uterine horn pregnancy requires keen suspicion and its management demands knowledge of the subject. To examine this problem a case will be presented and the literature reviewed.

Incomplete fusion of the mulliarian duct system with the formation of two uterine horns is responsible for this abnormality, as one of the horns remains rudimentary and does not participate in the formation of the cervix and vagina. The uterine tubes and ovaries are normal; but the urinary tract is frequently anomalous, too, indicating the close embryologic association of these two systems.

Pregnancy in a rudimentary horn is a rare occurrence. The first case was reported by Mauriceau in 1669.[1] There have been 329 cases reported, with an incidence of about 1 in 142,00 deliveries.[2] The pregnancy is more commonly found in the right horn.[3]

Fertilization may result from transperitoneal migration of either the sperm or the fertilized ovum. The former seems more likely, as the corpus luteum of pregnancy is found on the side of the rudimentary horn in 95% of the cases.[2] No communication between the rudimentary horn and the vagina has been reported in 11 out of 13 cases by one author.[4] John reported one patient in whom the rudimentary horn did not communicate grossly, but did communicate on microscopic examination; and he noted that this type of examination is not usually mentioned in the reported cases.[5] The improbability of transmigration has led Latto to believe that a canal is present at the time of fertilization but closes off due to the growth of the fibromuscular tissue of pregnancy.[6] Without this explanation it is difficult to account for the disposal of the menstrual blood. Followers of Sampson's theory of endometriosis would postulate that the gynatresia† of a rudimentary horn is associated with a frequent occurrence of endometriosis, and several such cases have been reported.[7] In 19 patients in one series reported by Gardner only five cases of endometriosis were diagnosed, which is less than the incidence of endometriosis in all gynecologic patients in the same hospital.[8]

If the communication with the uterus is through a small opening, one would expect dysmenorrhea. Indeed Merkal has reported 17 cases from the literature with dysmenorrhea and unilateral pelvic tumor. At laparot-

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*Presented at the Minnesota Obstetrical and Gynecological Society Meeting, St. Paul, Minnesota, December 7, 1963.

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†See Test Your Word Score Page 763.

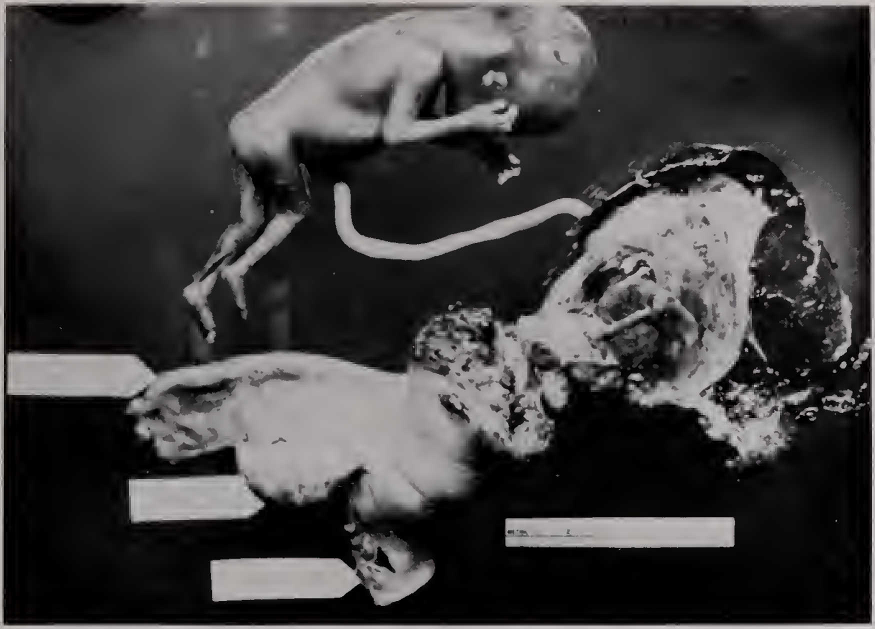

Fig. 1 — Resected rudimentary uterine horn with attached tube, ovary, and products of conception.

omy these patients were found to have a rudimentary horn with menstrual blood in the communicating horn. None of these patients was pregnant. Merckel named this the syndrome of unilateral gynatresia.[9]

The correct diagnosis of an intact rudimentary horn pregnancy is rarely made.[10] Abramson noted that since the horn is mobile and the gestation is late, a pelvic roentgenogram will show a fetal skeleton high in the abdomen. With this technique he diagnosed one of the few unruptured rudimentary horn pregnancies in the literature.[11]

The usual pregnancy complication is rupture of the horn, commonly occurring between the 16th and the 20th week of gestation and only rarely before the 12th week. This late rupture is attributed to the thick wall of the horn in contrast to the uterine tube. A high index of suspicion should be present in all ectopic gestations of more than 12 weeks. An occasional patient will manifest only mild symptoms and not be operated upon. At a later date, laparotomy for adnexal mass discloses a lithopedian with a healed ruptured rudimentary horn.[4] O'Leary reported a case of an abdominal pregnancy due to a healed ruptured rudimentary horn pregnancy which was carried to term and was delivered successfully by abdominal incision.[2]

The recommended procedure at laparotomy is removal of the ruptured horn and the accompanying uterine tube. The reason for removing the tube is to prevent future tubal pregnancies. January reported a patient with a ruptured rudimentary horn pregnancy where the accompanying tube and ovary were left in place. A subsequent pregnancy occurred in the noncommunicating uterine tube.[12] The main uterine defect should be closed in layers. Total hysterectomy need not be performed, as future pregnancies are possible in the remaining horn.[5] Several patients have been subjected to total hysterectomy because the condition was not recognized at the time of the operation.[4]

Case History

A 19-year-old white married female, who had had her last menstrual period on October 2, 1962, was admitted to the University of Minnesota Hospitals on January 18, 1963, with a history of morning sickness and breast engorgement. She had not seen a doctor for prenatal care.

Two days prior to admission, she had noted the onset of vague abdominal cramps radiating to both sides of the lower abdomen. The cramps continued and on the following day she had sharp lower abdominal pain associated with shoulder-strap pain. With the onset of nausea and emesis she sought medical advice. A private physician made a diagnosis of ruptured tubal pregnancy and referred her for treatment.

Her past medical history was normal. She denied any dysmenorrhea. Her physical examination including the pulse, blood pressure and temperature was normal with the exception of the pelvic and abdominal areas. The abdomen showed mild rebound tenderness and a mass consistent with a 20-week pregnancy. The fetal heart tones were inaudible and no fetal complexes were seen on fetal electrocardiogram. No adnexal masses were palpated. An irregular mass was present in the cul-de-sac. A culdocentesis produced blood.

Laboratory examination showed a hemoglobin of 8.7 grams % and a white count of 24,300. A chest film was normal. An abdominal film showed no fetal parts. The uterus could not be identified and the right psoas shadow was blurred.

Shortly after admission the blood pressure fell and blood was administered. At laparotomy the peritoneal cavity contained 2500 cc. of blood. A fetus, measuring 16 cm. from crown to heel and 11 cm. from crown to rump, was lying free in the peritoneal cavity with the placenta attached to the ruptured rudimentary horn of a bicornate uterus. The corpus luteum was on the attached ovary. The rudimentary horn was resected as well as the corresponding uterine tube (See Figure 1). A total of 3000 cc. of whole blood was replaced intravenously, and the postoperative course was uneventful.

Microscopic examination of the base of the horn showed no communication with the main part of the uterus. An intravenous pyelogram taken before discharge showed that the right kidney was ectopically low in the abdomen and there was duplication of the right ureter and the renal pelvis.

The patient returned to the prenatal clinic in her second pregnancy with an expected date of confinement of March 15, 1964. She had a normal prenatal course. On March 12, 1964, after a total labor of 11 hours and 17 minutes, she had an outlet forceps delivery of a normal 2680 gram male infant over a left mediolateral episiotomy using pudendal block anesthesia. The patient's post-partum course was normal.

Comments and Conclusion

This patient presented with the typical picture of a ruptured rudimentary uterine horn pregnancy. She was beyond 12 weeks' gestation and had the signs and symptoms of a ruptured tubal pregnancy. The lack of communication between the cervix and the horn on microscopic examination favors transmigration of the sperm. A urinary tract abnormality was demonstrated.

The subsequent delivery substantiates the necessity for conservative management.

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Man is the only animal that laughs and weeps; for he is the only animal that is struck by the difference between what things are and what they might have been.
— Hazlitt

Stay on course, the storm will soon be over. — C.O.R.

Experience with Pargyline Hydrochloride

(Nonhydrazine Monoamine Oxidase Inhibitor)

as an Antihypertensive Agent:

Preliminary Observations in 32 Patients*

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THE INTRODUCTION of pargyline hydrochloride for the treatment of hypertension represents a further effort to utilize an enzymatic blocking agent in the treatment of hypertension. Methyldopa, which interferes with the decarboxylation of dopa to dopamine in aromatic amine biosynthesis, was the first drug of this nature to become available commercially. Pargyline hydrochloride is a potent monoamine oxidase inhibitor of the nonhydrazine group first synthesized by Taylor.[1] The hydrazine structure (-NH-NH-), which was present in earlier monoamine oxidase inhibitors such as iproniazid, is not present in pargyline, and it had been suggested that this structural difference might decrease the likelihood of toxicity from the drug.[2] Pargyline is the first monoamine oxidase inhibitor to be introduced specifically as an antihypertensive agent, although the hypotensive effect of other monoamine oxidase inhibitors had been known previously. The drug is extremely effective in monoamine oxidase inhibition, but the exact manner in which it causes a lowering of blood pressure in man is not known.[3] As mentioned by Sjoerdsma,[2] the accumulation of various amines in the sympathetic ganglia or at the terminal nerve endings may be, in some manner, responsible for this effect.

Materials and Methods

This paper presents the data from 32 hypertensive patients who were treated with pargyline hydrochloride in the outpatient department of the Mayo Clinic. Of the 32 patients, 16 were men and 16 were women. The average age was 56, with ages ranging from 37 to 70 years. The Keith, Wagener, and Barker system of grading hypertensive retinal changes was used. Twenty-seven of the patients had group 2 hypertension, two had group 1, two had group 3, and one had group 4. Twenty-eight were classified as having essential hypertension, and four as having hypertension that was renal in origin (Table 1). Levels of blood pressure were determined daily in the sitting and standing positions for most patients during the initiation of treatment. Levels of blood pressure during the final or current period of treatment with pargyline were used in evaluating the results. The majority of the patients either had no previous treatment for their hypertension or had not received antihypertensive medications for at least several days prior to the initiation of therapy with pargyline. Twenty-two patients were treated initially with thiazide diuretics, to which pargyline was subsequently added. Five patients were treated with thiazide drugs in addition to another antihypertensive agent at the time pargyline was instituted (two with guanethidine sulfate, two with hydralazine hydrochloride, and one with reserpine). In five patients, treatment was started with pargyline hydrochloride alone. Serial determinations of hemoglobin levels, leukocyte counts, differential counts, serum glutamic oxaloacetic transaminase (SGOT) levels, blood urea values, and urine specimens were carried out for most of the patients.

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*Read at the meeting of the American Medical Association, San Francisco, California, June 21 to 25, 1964.

**Section of Medicine, Mayo Clinic and Mayo Foundation.

TABLE 1
Pargyline Hydrochloride: Clinical Characteristics of 32 Patients

Hypertension	Number of Patients
Cause	
Essential	28
Renal artery disease	3
Renal parenchymal disease	1
Retinal findings (Keith, Wagener, and Barker classification)	
Group 1	2
Group 2	27
Group 3	2
Group 4	1
Complications before treatment	
Ischemic heart disease	8
Azotemia (>50 mg. per 100 ml. of blood)	3
Cerebrovascular disease	3
Congestive heart failure	1
Period of observation, weeks	
50 to 55	2
40 to 49	1
30 to 39	3
20 to 29	5
10 to 19	4
5 to 9	3
4 or less	14

Early in the study, the initial drug dosage was 10 mg., given as one dose at bedtime, increased rather rapidly at two or three-day intervals in increments of 10 mg. The cumulative action of the drug soon became apparent, and the increments then were made at weekly intervals, with a usual starting dose of 25 mg. The average daily dose of pargyline for the entire group was 32 mg., with a range of 10 to 100 mg.

The clinical characteristics of the patients are summarized in Table 1. In seven patients, it was necessary to discontinue the use of pargyline because of side effects. Angina pectoris developed in one patient, and therapy was stopped after four days. The other six patients had shown reasonably satisfactory responses to the drug before it was discontinued because of side effects (insomnia in two, fluid retention in two, and congestive heart failure in two). Three patients receiving full doses of thiazide diuretics showed no apparent response to pargyline when it was added to the program; thus, the use of the drug was discontinued. In two others, tolerance developed to the medication and therapy was stopped: in one patient at six weeks and in the other at 28 weeks.

Results

The results of treatment with pargyline hydrochloride are summarized in Tables 2 and 3. The reduction of mean blood pressure was 10 per cent or greater in 19 of 31 patients; the patient in whom therapy was stopped after four days was not included in the total calculation of results.

Reduction of Blood Pressure

In patients treated with pargyline alone, the blood pressure decreased an average of 16 mm. Hg systolic and 10 mm. Hg diastolic. In patients receiving pargyline in addition to a thiazide diuretic, the blood pressure decreased an average of 20 mm. Hg systolic and 12 mm. Hg diastolic. In the patients receiving pargyline, a thiazide, and additional antihypertensive therapy, the average decrease of blood pressure was 40 mm. Hg systolic and 22 mm. Hg diastolic. The concomitant use of pargyline and other antihypertensive drugs had an additive effect in lowering blood pressure. This was most strikingly demonstrated in one patient who, at the time pargyline was added to her program, was receiving 450 mg. of guanethidine and 120 mg. of pentolinium tartrate (Ansolysen) in addition to a thiazide diuretic with poor control of her hypertension. Her blood pressure is currently under good control with 50 mg. of guanethidine and 100 mg. of pargyline daily, plus a thiazide diuretic.

Insomnia

The major and minor side effects precipitated by the use of pargyline hydrochloride are listed in Table 4. Insomnia and retention of fluid were the most common complaints. These side effects have been noted in most other reports.[4-8] In two patients, the use of the drug was stopped because of insomnia. The loss of sleep resulting from pargyline

TABLE 2
Pargyline Hydrochloride: Results of Treatment in 32 Patients[*]

	Blood Pressure, mm. Hg						Average Reduction in Mean, Per Cent
	Before Treatment			During Final Treatment			
Position	Systolic	Diastolic	Mean	Systolic	Diastolic	Mean	
Sitting							
Pargyline	171	103	136	155	93	124	8
Pargyline and thiazine	175	109	142	155	97	126	11
Pargyline, thiazide, and other agent	192	120	156	152	98	125	19
Standing							
Pargyline	174	104	139	152	92	122	12
Pargyline and thiazide[†]	159	104	132	142	94	117	11
Pargyline, thiazide, and other agent[†]	178	111	144	135	88	111	22

[*] One patient treated for four days is not included.

[†] No standing control available for eight patients.

TABLE 3
Pargyline Hydrochloride: Results of Treatment in 32 Patients[*]

		Reduction of Mean Blood Pressure, Per Cent			
Position	Number of Patients	39 to 30	29 to 20	19 to 10	Less than 10
Sitting					
Pargyline	4	1			3
Pargyline and thiazide	22		3	10	9
Pargyline, thiazide, and other agent[†]	5	1		4	
Standing					
Pargyline	4	1		1	2
Pargyline and thiazide[‡]	15	1	4	2	8
Pargyline, thiazide, and other agent[‡]	4	1	1	2	

[*] One patient treated for four days is not included.

[†] Two patients received guanethidine, two hydralazine hydrochloride, and one reserpine.

[‡] No standing control available for eight patients.

therapy was very disturbing to some patients, but administration of the dose in the morning did not seem to change the pattern of insomnia. One patient with pre-existing angina pectoris experienced anginal attacks of greater severity and frequency while being treated with pargyline hydrochloride, and another patient had symptoms of angina pectoris first appear after initiation of therapy.

Fluid Retention

The retention of fluid, as manifested by peripheral edema and rapid fluctuations in weight, was of particular concern to the women who underwent treatment. We believe that fluid retention resulted in the development of congestive heart failure in two patients. The concomitant use of a thiazide diuretic alleviated this difficulty to a certain extent but did not abolish it. Postural dizziness with near syncope occurred in three patients despite efforts to caution them concerning the orthostatic* effect of the drug. Our early, rather frequent increases in dosage may have been responsible for this effect in these patients.

Bronchial Spasm

One patient developed symptoms of bronchial asthma while being treated. This patient, a 64-year-old woman, had been maintained rather well with a thiazide diuretic and 10 mg. of pargyline daily. After a number of weeks of therapy, hospitalization was necessary because of an acute episode of severe wheezing. There was no previous history of asthma. Supportive measures to alleviate the bronchospasm were effective initially; but two weeks later a similar episode occurred, and the patient succumbed. Pargyline therapy had been continued until shortly before her death. While it is difficult to state unequivocally that a relationship to pargyline hydrochloride was present, no other therapy was given prior to the first asthmatic episode, and the sudden development of severe bronchospasm was most striking.

Minor Side Effects

Minor side effects were noted in five patients. These included dry mouth in two, faintness in one, constipation in one, and nausea in one (Table 3). None of these side effects, however, necessitated the stopping of the drug therapy.

A mood-elevating effect, while difficult to evaluate, was observed in some of the patients. This was noted particularly in one patient, who had become quite depressed during therapy with guanethidine.

During this study no abnormalities were found in results of serial laboratory determinations. In those patients with pre-existing azotemia,* aggravation of the nitrogen retention did not occur. The absence of laboratory data indicating hepatotoxicity may be a reflection of the nonhydrazine formulation of this drug.

Discussion and Conclusions

In 20 of the 32 patients, treatment with pargyline hydrochloride proved to be reasonably effective and was well tolerated by the patients. Nevertheless, unsatisfactory responses in 12 of the patients, either because of side effects, tolerance, or lack of antihypertensive action, emphasizes that, despite intensive research by pharmacologists and physicians, an ideal therapeutic agent for hypertension must still remain the hope for the future. More recent information concerning possible adverse reactions during the administration of monoamine oxidase inhibitors and the ingestion of aged cheese,[9] fermented beverages, or medications containing sympathomimetic amines should alert the physician to the need for caution when using this class

TABLE 4
Pargyline Hydrochloride: Side Effects in 23 Patients

Type	Number of Patients
Major	
Angina	2
Fluid retention	4
Insomnia	7
Congestive heart failure	2
Postural dizziness	3
Minor	
Dry mouth	2
Faintness	1
Constipation	1
Nausea	1

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*See Test Your Word Score Page 763.

of drugs in the treatment of hypertension. Admonition of the patient to avoid such exposures will never completely eliminate the possibility of their occurrence. With certain reservations, we believe that pargyline hydrochloride is a reasonably effective and well tolerated agent. Its use should be restricted to those patients with moderately severe hypertension and with evidence of good cardiac reserve. Patients who become depressed while being treated with other agents may be treated advantageously with pargyline, utilizing its mood-elevating effect. Because the mechanism of action is unknown and because of the potential development of unexpected reactions, the prescribing physician must attend the use of pargyline with greater than usual caution and observation. Continued study of the drug should help in delineating the place of pargyline hydrochloride in the treatment of hypertension.

Acknowledgments

Miss Karen Greenlee gave valuable technical assistance in data calculation, and pargyline hydrochloride was supplied for this study as Eutonyl by Abbott Laboratories, North Chicago, Ill.

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SUPRASPINATUS SYNDROME

This is a general term used to include a variety of lesions involving the subacromial bursa, the supraspinatus tendon, and may include tears, detachment, or calcification of the tendon, tendonitis, or lesions of the greater tuberosity.

Symptoms include aching in the region of the shoulder joint with referred pain into the neck, outer side of the arm, or dorsum of the forearm. There is loss of power and inability to initiate or sustain abduction. In the middle range of abduction, movement of the tendon may impinge on overlying processes and become compressed between the humerus and acromion, causing pain. Any movement may bring the lesion in contact with the acromion and causes muscle spasm. When this condition becomes chronic it may develop limitation of motion of the shoulder and disuse atrophy.

The prognosis in this condition is usually good. Surgical removal of calcium may be indicated, or the pinpoint area may be injected with hydrocortone. Bosworth, JAMA 117:422, 1941.

By taking revenge, a man is but even with his enemy; but in passing over it, he is superior. — Francis Bacon

IT'S THE LAW

Doctor Liable for Vocal Cord Paralysis Following Subtotal Thyroidectomy

The patient established a *prima facie* case of negligence, since it could be inferred from the facts that she had a soft, feminine voice before his performance of a subtotal thyroidectomy, but her left vocal cord was found to be permanently paralyzed immediately after the operation, that the doctor had severed or injured the recurrent laryngeal nerve, the Alaska Supreme Court ruled.

The doctor noted in his operative report that the recurrent laryngeal nerve was visualized on the right side. It was also noted in the report that there was a symmetrical marked enlargement of both lobes of the thyroid gland, but no mention was made of anything irregular in the recurrent laryngeal nerve's appearance or course.

The patient's evidence established that immediately after the operation her previously soft, feminine voice was hoarse and that this condition has persisted. Postoperative examination disclosed that her left vocal cord was permanently paralyzed and there was expert testimony that the hoarseness indicated that the recurrent laryngeal nerve was injured in the operation.

The doctor's operative report, which was not dictated until the day after the operation, merely stated the ultimate facts connected with each step of the operation on the right side and noted that the same procedure was followed on the left side, without specifically stating that the recurrent laryngeal nerve was visualized on the left side.

The patient contended that the operation was performed without her informed consent. She testified that the referring doctor told her that the operation was nothing more than a tonsillectomy and that she might not have consented to it if she had been informed of the risk of losing her voice. A doctor does not have to inform a patient of all the risks involved in an operation but may tailor his warning to the particular patient, the court said.

The patient contended that the doctor's operative report should not have been admitted in evidence because, having been made after he knew her voice was not normal, it was self-serving. The admission of the report was not prejudicial to the patient. There was no jury to be misled, the record indicated that the trial judge used abundant caution in admitting it, and there was nothing in the report itself that was prejudicial.

Patrick v. Sedwick, 391 P.2d 453 (Alaska, April 21, 1964) — Citation Vol. 10, No. 2

Early Anglo-Saxon Pharmacopeia*

Yarrow: For toothache, take a root of this wort; give it to eat fasting. . . . For wounds which are made with iron, take this same wort, pounded with grease; lay it to the wounds; it purgeth and healeth the wounds. . . . In case that any man with difficulty can pass water, take juice of this same wort with vinegar, give it him to drink; wondrously it healeth.

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*See Minnesota Med May 1965, Page 587.

A saint is a sinner who keeps on trying. — The Upper Room

Diabetes Mellitus and Surgery

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PATIENTS WITH diabetes mellitus may develop any of the diseases for which major or minor surgical procedures are required. Additionally, the diabetic patient is particularly prone to gangrene of the extremities, cholelithiasis and cholecystitis, carbuncles, and other suppurative processes such as perinephric abscess. The intervention of a disease process which may require surgery frequently demands changes in the traditional pattern of management of diabetes in both the preoperative and postoperative periods.

Moreover, because of the development of complications of diabetes mellitus and due to the nonspecific stress of surgery, the diagnosis of diabetes may be first entertained when the patient is admitted to a surgical service. In a recent review,[1] newly discovered diabetes was found in 23 percent of 487 patients undergoing surgical procedures. In view of these data which confirm the experience of others, it would appear that screening for diabetes by the determination of the fasting and two-hour postprandial blood glucose, particularly in these patients over the age of 40, would be a highly desirable preoperative measure. It should be emphasized that patients admitted to emergency wards frequently receive glucose solutions intravenously shortly after admission. In such instances, glucosuria noted in the first urinalysis may be disregarded and the diagnosis of diabetes mellitus mistakenly overlooked.

On the other hand, the urinalysis may be negative for glucose when the so-called "renal threshold" for glucose is elevated. It should be noted that the "renal threshold" is not a single variable but is dependent upon three variables. These are the tubular reabsorptive capacity for glucose, the glomerular filtration rate, and the arterial plasma concentration of glucose. Under circumstances during which the glomerular filtration rate may be further reduced by decreased renal perfusion pressure due to anesthesia or unrecognized plasma volume depletion, the urine may be free from glucose even in the presence of moderate hyperglycemia.

Influence of Diabetes Mellitus on Diseases Requiring Surgery

Increased mortality and morbidity are well recognized phenomena in diabetic patients undergoing surgery.[1,2] The chief factors in the increase are as follows:

1. The degree of control of the diabetes, particularly the presence or absence of ketoacidosis; 2. the prevalence of vascular disease; 3. the greater susceptibility of the diabetic patient to infection.

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Vascular Disease

Generalized vascular disease is more common in middle-aged and elderly diabetic subjects than in nondiabetic subjects of the same chronological age. Younger patients with diabetes of long duration may also have generalized vascular disease involving the cerebral, coronary, renal, and peripheral arteries. Although it is to be readily expected, it is not generally appreciated that vascular accidents following surgery are more common in diabetic patients. Acute myocardial infarction and congestive heart failure as a manifestation of coronary insufficiency are particularly prone to occur postoperatively. The precipitating factors are probably multiple in origin. Periods of hypotension during anesthesia and surgery may cause decreased perfusion of diseased vessels. The clinical manifestations of cerebral, myocardial, and renal ischemia may then be noted postoperatively. Uncontrolled diabetes, especially in the presence of diabetic keto-acidosis, may be associated with large extracellular and plasma volume deficits. Hypotension may or may not be present, depending upon the degree of peripheral and splanchnic vasoconstriction. Failure to correct the volume deficits will cause decreased cardiac output and result in decreased organ perfusion. The same phenomena may occur after surgery if the management of the diabetes is grossly inadequate.

Infections

Although increased susceptibility of the diabetic patient to infection has long been a clinical axiom, the pathogenesis is poorly understood. In patients with poorly controlled diabetes it is possible that this merely represents decreased resistance secondary to negative nitrogen balance, derangement of electrolyte and water balance, and disordered cellular metabolism. In patients with diabetic keto-acidosis, increased plasma adrenal-corticosteroid concentrations may also play a role. It is further conceivable that there may be disorders of the immune mechanism which are a fundamental part of the diabetic disease process.

Influence of Surgery on Diabetes Mellitus

Uncontrolled diabetes is readily precipitated by most surgical diseases. Superimposed upon already existent insulin insufficiency are the hyperglycemic effects of stress.[3] The stress reaction is characterized by increased sympathicoadrenal and adrenal corticosteroid activity. The resultant increase in circulating epinephrine causes the breakdown of liver glycogen and further increase in blood glucose. The increase in plasma glucocorticosteroids results in increased production of glucose from protein stores (gluconeogenesis). General anesthesia itself undoubtedly contributes to the impairment of carbohydrate metabolism, although the specific effects of various anesthetic agents are a matter of controversy.[4] The ultimate effects of the surgical diseases, of anesthesia, and of surgery are further impairment of carbohydrate metabolism and an increase in insulin requirements.

Management of the Diabetic Patient During the Surgical Period

The goal of management of the diabetic patient during the three phases of the surgical period is the maintenance of metabolic homeostasis. Three factors which must be considered in the attainment of this goal are the avoidance of keto-acidosis, the prevention of hypoglycemia, and the correction of electrolyte and water deficits. It is readily apparent that concomitant cardiovascular renal disease, anemia, and infection must also be carefully evaluated and vigorously treated prior to surgery.

Depot Insulin vs. Regular Insulin

A difference of opinion exists as to the use of depot insulin or regular insulin on the day of surgery and postoperatively. Advantages and disadvantages can be noted with either therapeutic program. Some competent authorities[3,5] prefer NPH insulin with supplementary doses of regular insulin as required, while others[6,7] prefer the administration of crystalline insulin at specific intervals. Both modes of therapy have been used successfully in our Medical Center. It would appear that careful evaluation of the total patient and the adoption of a specific therapeutic program tailored to the patient is of greater importance than the type of insulin which one selects for therapy. Failure of total patient evaluation and lack of appreciation of the goals of therapy may lead to tragic consequences and may, indeed, be lethal. The proper therapeutic philosophy has been superbly summarized by Rynearson[8] who stated that "while many surgical conditions require special attention, diabetes requires only constant attention."

Guidelines for Proper Therapy

1. Total patient evaluation is absolutely essential to proper diagnosis and therapy. A precise history and a meticulously performed physical examination are of major importance.

Case History

A 21-year-old man with diabetes of five years' duration was admitted with diabetic coma. The presence of abdominal rigidity and the absence of bowel sounds suggested the possibility of intra-abdominal disease. A careful history from the mother revealed that intense headache, fever, nausea, and vomiting had been present for 36 hours prior to the onset of coma. Physical examination revealed nuchal rigidity. Clinical workup led to a diagnosis of meningococcal meningitis. Proper therapy of the meningitis and diabetic coma led to recovery.

2. Diabetic keto-acidosis may simulate numerous types of acute surgical diseases of the abdomen. This may occur with or without acute gastric dilatation. In some instances the history and physical examination may help delineate the two conditions. In other instances the diagnostic dilemma may not be solved until the keto-acidosis has been successfully treated.

3. Surgery should never be performed on a patient with classical diabetic coma before therapy has corrected the metabolic defects and before a definitive diagnosis is reached.

4. The urgency of emergency surgery is frequently overemphasized and such surgery is too frequently performed before adequate total patient evaluation and the therapy related thereto are carried out.

5. Treatment of infection and the drainage or removal of suppurative foci may be followed shortly by a dramatic reduction of insulin requirements.

6. Hypoglycemia may be readily overlooked in patients with complex symptoms and findings. The highest incidence of hypoglycemic reactions occurs in those patients who have received NPH insulin with supplementary doses of regular insulin.

7. The minimal definitive surgical procedure of the shortest duration should be performed. Regional or spinal anesthesia should be used wherever feasible. Early ambulation and early resumption of oral feedings may facilitate the control of the diabetes.

Management of the Nonketonic Diabetic Patient for Elective Surgery

Preoperative Cautions

The patient may continue on his usual treatment until the day of surgery, although some increment in insulin dosage may be necessary because of physical inactivity during the preparatory period. It is well to obtain a fasting blood glucose and serum electrolyte determinations as baseline studies prior to surgery. Accurate daily weights should be recorded during the preparatory period and continued during the postoperative period. Such records are absolutely mandatory* for proper fluid therapy.

Day of Surgery

On the day of surgery the therapeutic regimen of Duncan[6] is preferred. There are, however, no serious objections to other therapeutic programs[1,5] which utilize long-acting insulin. The possibility of hypoglycemia must be kept constantly in mind, particularly when supplementary doses of regular insulin are given later in the postoperative period. One fourth of the previous day's insulin dosage is given subcutaneously as crystalline insulin on the morning of surgery just prior to the administration of one liter of ten-percent glucose in water, administered intravenously at the rate of 20 to 30 drops per minute. Fifty grams of glucose are administered intravenously every six hours postoperatively in a volume calculated to meet the daily fluid volume requirements. This is preceded by the subcutaneous injections of one fourth of the previous day's dosage of insulin. Increments or decrements in insulin dosage are determined by the clinical course, as monitored by blood and urine glucose determinations and by the presence or absence of ketonuria and ketonemia. It will not generally be necessary to give sodium chloride during the first 24 hours, but this should be given subsequently to replace calculated deficits. Approximately 60 to 100 milliequivalents of potassium per day are required to prevent potassium depletion. The determination of the urinary concentration of sodium and potassium is a useful guide to the daily requirements for sodium and potassium replacement. Rigid control is not sought nor is it desirable. When oral feedings are resumed, they are administered every six hours according to the same plan until the patient can again receive his customary diet and insulin therapy.

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*See Test Your Word Score Page 763.

Management of the Diabetic Patient for Emergency Surgery When Diabetic Coma is Present

It is obvious that emergency surgery can not be performed in a patient in diabetic coma irrespective of surgical indications.

Guidelines for Therapy

1. Adequate regular insulin must be given early. In our clinic, we customarily give 100 units of regular insulin subcutaneously and 100 units intravenously as soon as the diagnosis is made. Further insulin dosage is determined by monitoring the patient at two-hour intervals with blood glucose and urine glucose determinations. The serum acetone test serves as a useful guide in estimating the requirements for insulin.

2. Isotonic saline is nonphysiologic. Isotonic saline contains 154 meq./L. of sodium and 154 meq./L. of chloride and is therefore markedly hypertonic as regards the chloride ion, and slightly so as regards the sodium ion. The administration of a solution with such an anion concentration is decidedly unphysiologic in a patient who is already in metabolic acidosis. Water and electrolyte replacement is carried out with a diabetic repair solution consisting of 500 ml. of saline, 500 ml. of distilled water, and one ampule of sodium bicarbonate containing 44 meq. The ionic content of this solution in milliequivalents per liter of solution is as follows: sodium 122, chloride 77, and bicarbonate 44.

3. Sodium bicarbonate is indicated early. The studies of Kety[9] have indicated that survival in diabetic coma is largely determined by the degree of reduction in cerebral oxygen utilization. This is correlated with the reduction of blood pH. Kety's results demonstrate that it is possible to bring the blood pH toward normal quickly by giving small amounts of sodium bicarbonate intravenously.

4. Glucose is not indicated early. The administration of glucose early will further increase the hyperosmolarity of the extracellular fluid and thus increase cellular dehydration.

5. Water loss may amount to seven to ten percent of the body weight.

6. Potassium replacement need not begin until the fourth to eighth hour of therapy, since the initial serum potassium is usually elevated. The elevation of the serum potassium initially in the face of an actual cellular deficit of potassium is due to the shift of potassium from the cells to the extracellular fluid, while hemoconcentration and poor renal function are present. This may be given by either the oral or intravenous route. If intravenous administration is required, 60 meq./L. may be given in a three to four-hour period.

7. Plasma or whole blood may be indicated to combat shock.

8. Overhydration should be avoided.

After successful therapy of the diabetic coma, total patient evaluation can then determine whether emergency surgery is required.

Summary

1. Newly discovered diabetes is frequently encountered on a surgical service due to the nonspecific stress of surgical diseases and the resultant impairment of carbohydrate metabolism, and due also to diabetic

complications which require surgery for their correction.

2. Total patient evaluation by precise history, a careful physical examination, and indicated laboratory studies are imperative before any surgical measures are taken.

3. Metabolic defects should be corrected as nearly as possible before surgery is performed.

4. The goals of therapy postoperatively are the avoidance of keto-acidosis and hypoglycemia and the prevention of electrolyte and water imbalance.

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WHAT'S YOUR DIAGNOSIS?

A fifty-five-year-old executive complained of right lower abdominal pain of three days duration. Initially it was associated with an urge to move his bowel, but normal daily bowel movements did not alter the pain. He had no nausea, dysuria, or fever, and his appetite remained normal. One month previously he had noted a similar episode of pain which had spontaneously subsided in two days. Except for an uneventful repair of a left inguinal hernia six months previously, he had been in good health.

Physical examination disclosed an afebrile man in no acute distress. There was tenderness and guarding in the right lower abdomen, but no abnormal masses were palpated. Bowel sounds were normal and there was no rebound tenderness. Rectal examination aggravated the pain, particularly on the right.

Admission chest X ray, hemoglobin, and urinalysis disclosed no abnormality. The leucocyte count rose from 12,000 to 14,000 overnight, with a relatively normal differential. Exploration was carried out. A normal appearing appendix was found lateral to the hepatic flexure.

What is your diagnosis? See page 746.

An admirer once asked James Barrie how he managed to grow old so gracefully. He answered, "My dear lady, I give all my time to it." — Walter Winchell

For just experience tells, in every soil, That those that think must govern those that toil. — From The Traveller — Oliver Goldsmith

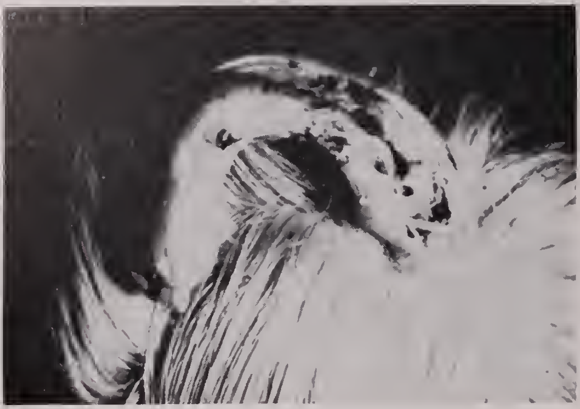

Fig. 7 — Cutaneous horn. The scalp is a common location.

Precancerous

THE TERM "precancerous" has been used loosely by dermatologists to include dermatoses in which the incidence of carcinoma is no greater than should be expected when various factors such as age, exposure to sunlight, chronic irritation, and effects of previous treatment are considered. The term "precancerous" dermatosis should be confined to true but rare instances of Bowen's disease, various types of leukoplakia, senile keratosis, cutaneous horn, and keratosis resulting from the ingestion of arsenic, exposure to tar, and iodizing radiation. In at least 20% of these disorders carcinoma eventually develops and is usually of the squamous-cell type. In the past, other diseases such as seborrheic keratoses, certain nevi, tuberculous and stasic ulcers, lupus vulgaris, lupus erythematosus, epidermal cysts, and scars following burns have been incorrectly labeled precancerous, since the incidence of carcinoma varies from only a fraction of 1% to about 5% in these disorders. If the term precancerous is used as it has just been defined, it has a meaning both clinically and histologically, and is of value from the standpoint of prognosis and treatment.

Bowen's Disease

Bowen[1] (1912) described two cases in which there was a solitary lesion which resembled a noduloulcerative syphilid, and he stated that the disorder was a precancerous dermatosis. The early nodular lesions became dull red, infiltrated, crusted plaques by peripheral extension followed by superficial ulceration. A rolled pearly border was rarely present.

The disorder occurs usually on the trunk, although the face and extremities may be involved. In one of Bowen's cases the disease persisted for 19 years without increase in the size of the lesion or development of metastasis. Subsequently, however, many cases have been reported in which squamous-cell epithelioma developed with metastasis and death. The term precancerous dermatosis of Bowen should be limited to lesions which resemble a noduloulcerative syphilid. There have been many cases reported as Bowen's disease which were in reality examples of superficial epitheliomatosis.

Surgical excision or electrodestruction are the methods of choice in the treatment of the disorder. The lesions are relatively radioresistant, hence radiotherapy is usually contraindicated. However, it is of value occasionally in superficial plaques.

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Dermatoses*

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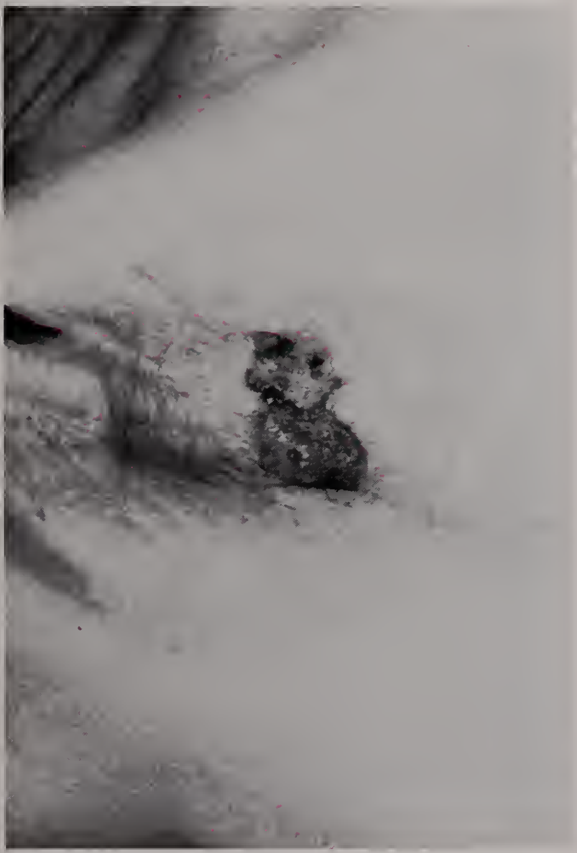

Fig. 1 — Bowen's disease in the axilia. The arcuate nodular lesion simulates a tertiary syphilid.

Leukoplakia

The term leukoplakia is derived from the Greek, meaning white plaque. The word leukokeratosis implies that the lesion has become thickened and elevated.

Leukoplakia usually occurs on the inner surfaces of the lips and cheeks and on the dorsum and edges of the tongue. The disorder is not confined to the oral cavity and may occur on the male and female genitals. The lesions are usually dull white and occur as patches, isolated points, or bands. The incidence of carcinomatous change in leukoplakia is difficult to determine but has been estimated to be from 20 to 30%.

Leukoplakia results from chronic irritation and trauma such as smoking, jagged or carious teeth, and poorly fitting dentures. About 95% of the cases occur in men. Women who have the disorder usually have improperly fitting dentures or are heavy smokers. Syphilis as an etiologic factor is unimportant.

Treatment consists of the removal of local irritants, proper adjustment of dentures, cessation of smoking, and proper care of the teeth. Lesions which become verrucous, fissured, or ulcerated should be destroyed by electrodesiccation or cauterization. They are radioresistant. Surgical removal is occasionally indicated when the lesions are extensive.

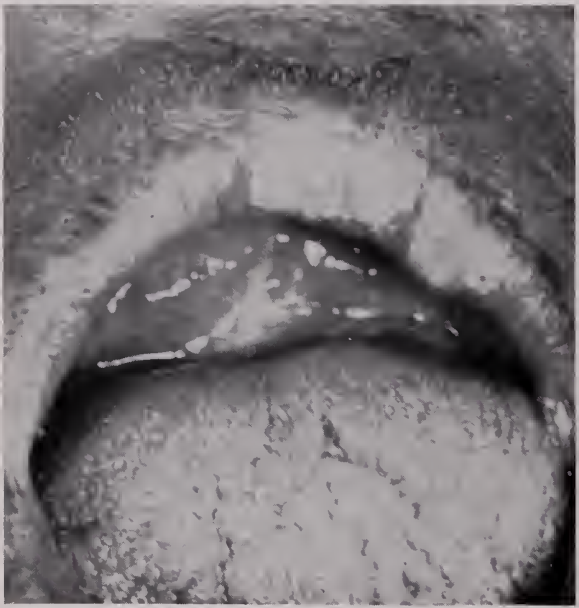

Fig. 2 — Extensive leukoplakia of the upper lip. The lower lip is involved more frequently.

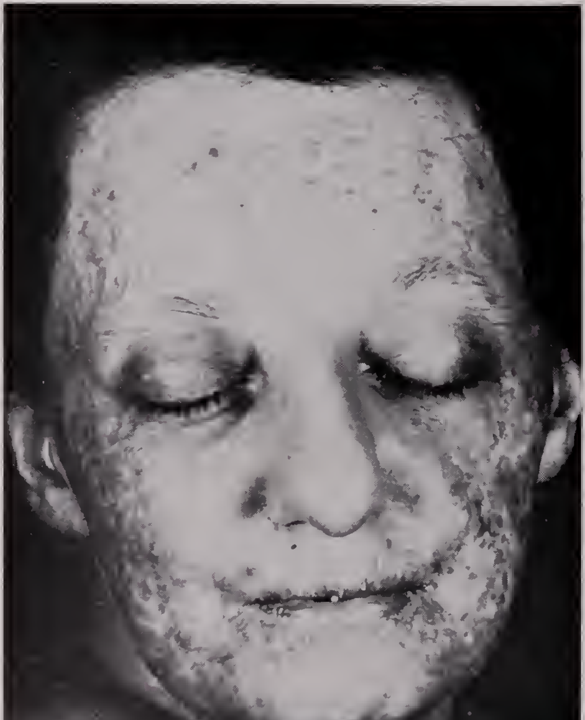

Fig. 3 — Chronic radiodermatitis showing hyper and hypopigmentation and numerous keratoses.

Radiodermatitis

Acute Type

First degree radiodermatitis consists of erythema with slight burning, itching, and scaling which disappears after a few days or weeks. There may be temporary alopecia, and pigmentation may develop later.

In second degree radiodermatitis there is edema, intense erythema and vesiculation. In a few days exudation, erosion, and crusting ensues. There is a loss of hair which may be permanent. The activity of the sebaceous and sweat glands is impaired. Atrophy and telangiectasias appear several months later.

Third-degree radiodermatitis is characterized by necrosis and ulceration. Healing is usually slow and may take several months; in some instances the ulcerations are so indolent that they never heal.

Chronic Type

This form of radiodermatitis may develop after the acute type or insidiously as a result of an excessive number of fractional (suberythema) doses. The skin is dry, thin, smooth, shiny, and sensitive to trauma. Itching and burning are prominent symptoms. There is both hyper and hypopigmentation and telangiectasia. The nails may be striated, discolored, brittle, or lost. As the disorder progresses multiple keratoses appear. Carcinoma develops in about 20% of the cases in which the damage has been greater than just simple telangiectasia. It is usually squamous rather than basal cell in type. Sarcoma may arise in areas of radiodermatitis.

The simpler forms of radiodermatitis can be treated successfully with measures which are used for corresponding phases of dermatitis due to other causes. Ointments or creams containing a steroid and an antibiotic are helpful in first degree radiodermatitis. If vesiculation is present moist compresses of Burow's solution may be employed. In severe cases where there is necrosis and ulceration, excision of the entire lesion followed by grafting is indicated. The procedure should be employed many months after the beginning of the dermatitis when progression has ceased.

Keratoses

Arsenical Type

Keratoses which follow the ingestion of inorganic arsenic appear as discrete, warty lesions usually on the palms, fingers, and soles. They are generally symmetric and surmounted by a small, black shiny peg of keratin. Fissuring is common. Keratoses following the ingestion of organic arsenic such as arsphenamine are rare but have been reported. Keratoses may develop within a month after the first ingestion of arsenic or as long as 30 years later. Once the lesions appear they usually persist and 20% of the cases eventuate in epithelioma even though there is no further ingestion of arsenic. There seems to be an individual susceptibility or tolerance to arsenic, because some patients are able to take the drug for many years with only mild pigmentation and keratoses, while others develop keratoses and epitheliomas followed by metastasis and death with only small amounts of the medication.

Treatment for arsenical keratoses is unsatisfactory. When epithelioma develops, surgical excision is the method of choice. In some cases when carcinoma is present on a digit or on the palms and soles, amputation may be necessary.

Seborrheic Type (*Verruca Senilis*)

Seborrheic keratoses are not precancerous but should be discussed briefly because they are confused sometimes with senile keratoses. The former are more superficial and softer than the senile type. Seborrheic keratoses as a rule are multiple and are raised slightly above the surface of the surrounding skin. Their color varies from light brown to almost black, and they usually occur on the face, back, and chest. Removal of the loosely attached greasy crusts reveals a raw pulpy base. They begin in middle age. Carcinoma develops in only 1 or 2% and is almost always of the basal-cell type.

Seborrheic keratoses should not be treated with X rays or radium; they can be destroyed easily by means of cauterization or desiccation.

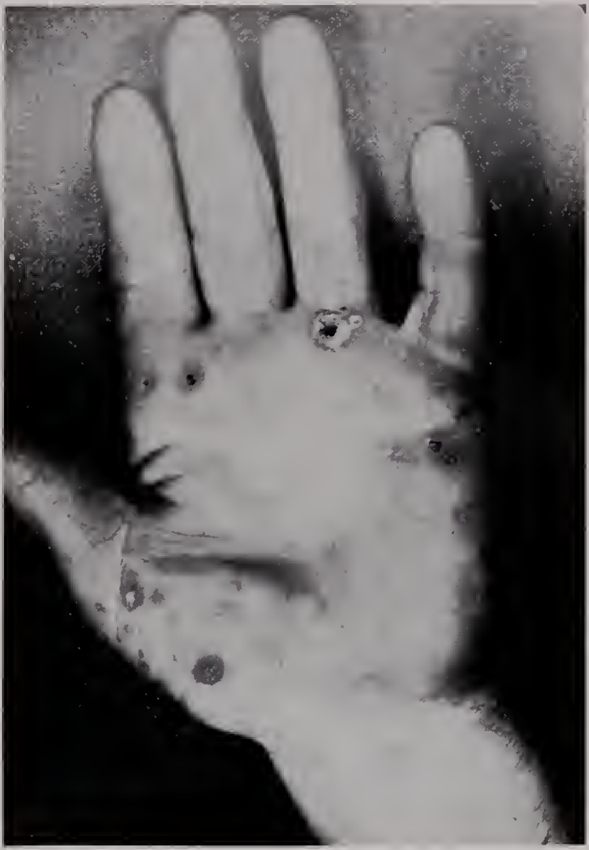

Fig. 4 — Arsenical keratoses. The lesions mimic ordinary warts.

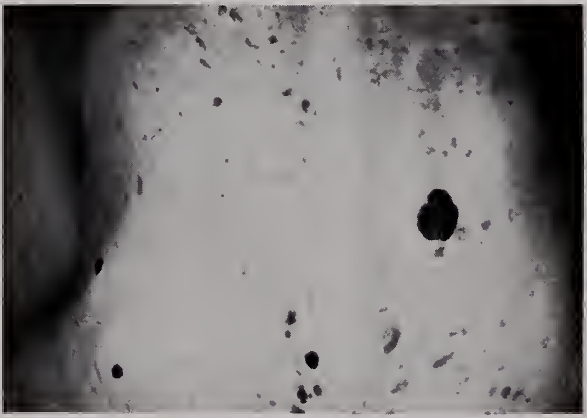

Fig. 5 — Multiple seborrheic keratoses on the back. These lesions should not be regarded as "precancerous."

Senile Type

These lesions are seen most frequently in people who have exposed to sun and wind for many years, and appear chiefly on exposed parts, especially the hands and face. They may be single or multiple and are usually dark brown or black. The surface of the

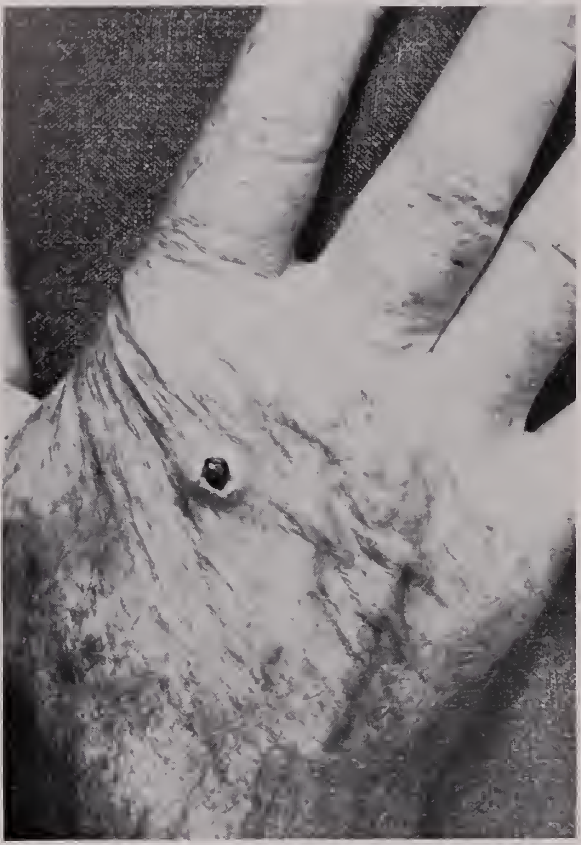

Fig. 6 — Senile keratosis plus early squamous-cell epithelioma.

involved skin is uneven, bleeds easily, and is sometimes superficially ulcerated. Senile keratoses are firmer, more discrete, and more raised from the surface of the skin than seborrheic keratoses. In 20 to 25% of the cases squamous-cell carcinoma develops in one or more of the lesions.

Senile keratoses are radioresistant and should be destroyed by means of cauterization or desiccation.

Cutaneous Horn

These lesions are rare and may resemble similar growths in lower animals. The majority of cutaneous horns develop from senile keratoses, and epitheliomatous changes occur frequently. Cutaneous horns are similar to senile keratoses except that there is an excessive development of keratotic material. They may be cylindric, straight or twisted, and usually occur on the scalp and face, although sometimes other areas are affected. The color varies from light brown to black. They may be short or several inches long.

Treatment is essentially the same as for senile keratosis. If the horn is small and shows no evidence of carcinoma it may be destroyed by cauterization or desiccation. A larger lesion, especially one in which malignant change is suspected, should be excised.

Reference

1. Bowen, J. T.: Precancerous Dermatoses: A Study of Two Cases of Chronic Atypical Epithelial Proliferation. J Cut Dis 30:241, 1912.

ANSWER TO WHAT'S YOUR DIAGNOSIS

(From page 741)

A large infarcted appendices epiploicae was found originating from the sigmoid colon.

The next time you hurry and press for time, remember the Egyptian mummies. They were pressed for time, too. — Banking

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With some people you spend an evening — with others you invest it.

— Santa Fe Magazine

Faith is the substance of things hoped for; the evidence of things not seen.

— The Bible

Gastric Cancer*

Treatment of

GEORGE T. PACK, M.D.**
IRVING M. ARIEL, M.D.**
New York, New York

CANCER OF the stomach accounted for 21,522 deaths in the United States in 1957 and for 1,538 deaths in New York City in 1957. The incidence of this neoplasm is three times as great in Japan, Finland, and Chile as in England, Canada, and the United States. Trapeznikov reports that gastric cancer is the most frequent malignant tumor in the Union of Soviet Socialist Republics, accounting for 30 per cent of all cancers.

Decline in Stomach Cancer Rates

The decline of stomach cancer in the United States and 23 foreign countries has been confirmed by William Haenszel of the Biometry Branch of the National Institutes of Health, U.S.A. Some of his key findings may be adumbrated as follows:

1. A steady decline in stomach-cancer rates in the United States for both men and women during the past several decades, a trend duplicated in some, but not all, foreign countries. (Age-adjusted rates per 100,000 for the United States were 28.8 in 1930, 26.5 in 1935, 22.5 in 1940, 19.9 in 1945, 16.0 in 1950, and 13.0 in 1955.)

2. A probable excess in the rates for certain foreign-born groups living in the United States over those of the native-born population.

3. An inverse relationship with socioeconomic status, with little evidence of specific occupational effects.

4. Great variation in stomach-cancer rates among countries.

5. Stable male-female ratios of rates for each country over the entire range of stomach-cancer rates.

6. Lack of marked urban-rural differentials.

7. The tendency for countries in northern latitudes to have higher rates, and the presence of north-south differences within the United States compatible with the broader international pattern.

Segmental Distribution of Cancer Within the Stomach

The location of the cancer in the stomach has a pertinent bearing on the operability and the choice of operative procedure. The lesser curvature has a special predilection for the site of gastric cancers, and the distal segment, namely, the pylorus and antrum, contains the majority of these new growths. However, they may occur in any portion of the stomach between the cardia and the pyloric ring. We have found an approximate frequency of involvement for the different segments of the stomach as illustrated in this table.

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*Presented at the Postgraduate Symposium, University of Minnesota, May 17, 1963.

**From the Pack Medical Foundation, Inc., New York, New York.

TABLE I

	Our Series	L C H & C[18]
Pylorus and antrum	45%	70%
Pars media	25%	14%
Cardia or proximal segment	12%	13%
Greater curvature	6%	—
Total or diffuse	12%	—
Esophagogastric junction	—	13%

About 75 per cent of gastric cancers arise from the distal half of the stomach, and these are cured more frequently than those of the fundus or those that are diffuse.

Distribution of Metastases from Gastric Cancer

Patterns of Distribution

In approximately 11 per cent of the patients with gastric carcinoma, the initial physical examination will present clinical evidence of metastases to regions that permit an immediate prognosis of inoperability and incurability, e.g., the perirectal tissues (rectal shelf of Blumer), the signal node of Virchow-Troisier, the palpable nodular liver, diffuse lymphatic pulmonary carcinosis, ascites, the umbilical nodule, remote nodal metastases to such sites as the inguinal and femoral groups, and the Krukenberg tumor of the ovary.

Blood-Vessel Invasion

Meissner demonstrated blood-vessel invasion in 57 per cent of patients with gastric cancer. He was unable to prove any correlation between the extent of metastases to lymph nodes and blood-vessel invasion, and no apparent relationship to the gross or microscopic types of the primary cancer in the stomach.

Metastasis to Perigastric Lymph Nodes

Coller reported involvement of lymph nodes in 75 per cent of his patients. Microscopic examination of the nodes frequently revealed metastases that were not apparent on gross inspection. There was no correlation between the size of the nodes and the presence or absence of metastases in the nodes. In Coller's experience, the polypoid gastric cancers produced lymphatic metastases in 60 per cent of cases, and the diffuse or invading cancers in 95 per cent. In due course of time and with continued active growth of the cancer, the metastases extended far beyond the perigastric nodes to involve nodes in the hilus of the liver, the para-aortic nodes, etc.

Cancers involving the distal gastric segment, particularly of the prepyloric region and antrum and converging on the lesser curvature, metastasize to lymph nodes along the hepatic pedicle in about 40 per cent of the patients with gastric cancer.

The "second-look procedure" of Wangensteen and associates revealed a high incidence of metastases to lymph nodes in the region of the hepatic pedicle and the retropancreatic site. Arhelger disclosed that when these sites are dissected from their lymph nodes, the involvement of regional nodes from gastric cancer reaches the high incidence of 90 per cent.

Perisplenic lymph nodes were involved by carcinoma from the stomach in 20 per cent of 63 cases reported by Zdeněk and Dvořáček, who stress dissection en bloc of the lineal vessels and contiguous tissues, with splenectomy and extended gastrectomy.

Significance of Supraclavicular Signal Node

In 1848, Virchow described metastasis to the supraclavicular fossa in the presence of abdominal cancers. Troisier in 1849 published a study of 27 primary abdominal cancers, the majority in the stomach, which had metastasized to supraclavicular lymph nodes. The eponyms* of Virchow's and Troisier's node have found popular usage to this day.

Viacava and Pack found that 23 (2.6 per cent) of 883 patients with gastric carcinoma had obvious metastatic involvement of the signal node, and in 17 of the 23 patients the recognition of this abnormal node was the first evidence of the cancer. In fifteen patients the left supraclavicular node was involved; in three patients, the right node; and in five patients the metastases occurred bilaterally to the neck. The route of metastasis is along the various lymph vessels to the perigastric lymph nodes and the coronary, celiac, and superior mesenteric nodes. By way of the truncus intestinalis the cancer emboli enter the cisterna chyli, travel upward along the thoracic duct, and enter the systemic venous circulation at the left side of the base of the neck.

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*See Test Your Word Score Page 763.

Metastasis to the signal nodes connotes a poor prognosis with no possibility of curative treatment. Biopsy of the left scalene node can reveal occult metastasis to the supraclavicular region and prevent needless exploratory laparotomy in selected instances.

Frequency of Various Symptoms

In approximately 0.5 per cent of the patients, there are no symptoms (asymptomatic or silent gastric cancer). Few significant differences exist in the frequency of each symptom with the exception of *dysphagia,* which occurred twice as often in patients with inoperable cancer as in those with resectable tumor. Dysphagia is more frequent in cancer of the cardia. Cancers in this location show a 20 per cent higher resectability because they apparently often manifest their presence early by dysphagia. Other symptoms are indicated in this table:

TABLE 2
Frequency of Symptoms

Weight loss	56-96%
Abdominal pain	22-96%
Vomiting	59-90%
Constipation	8-80%
Anorexia	17-82%
General indigestion	40-69%
Nausea	20-69%
Hematemesis	7-34%

The fact worthy of emphasis is that few significant differences in the incidence of various symptoms exist between patients with operable and those with inoperable gastric cancer.

The incidence of the first symptom experienced by the patient reveals no significant feature relative to operability.

Culpability for Delay in Diagnosis

Twenty years ago Pack and Gallo analyzed a large number of case records of cancer in an attempt to determine the responsibility for the delay in treatment. A delay of three months or more from the time of discovery of symptoms to the visit to the physician was regarded as undue delay on the part of the patient (Table 3). Criticism of the physician was based on the action taken by the first physician consulted. Leach and Robbins, using the same source material, showed improvement in the alertness of the patient but the same, or uncorrected, culpability on the part of the physician.

TABLE 3
Delay in Diagnosis

Due to patient	44.3%
Due to patient and Physician	18.0%
Due to physician alone	17.0%
No delay	20.7%

Relation of Gastric Ulcer to Gastric Cancer and Factors Influencing Treatment

In this controversial problem, there seem to be two important questions: (1) the diagnostic problem, which involves the clinical, gastroscopic, radiologic, and pathologic differentiation between gastric ulcer and ulcerocancer; and (2) the etiologic problem, involving the possible relationship of ulcer and ulcerocancer of the stomach, the consideration of precancerous lesions common to the two diseases, and the question of cancerous transformation of a benign gastric ulcer. First to distinguish between chronic ulcer and cancer of the stomach was Matthew Baillie of London who, in 1818, wrote his thesis on "The Morbid Anatomy of Some of the Most Important Parts of the Human Body."

The two accepted varieties of simple peptic ulcer are (1) the superficial type, which is not penetrative and is not to be confused with ulcerocancer, and (2) the deep, chronic peptic ulcer that does penetrate through the wall of the stomach and may simulate cancer in many aspects. The chronic gastric ulcer has steeply inclining walls with overhanging margins, and the circumferential mucosa is relatively normal. The two varieties of ulcerating cancer are (1) the ulceration of a fungating exophytic* cancer in which the ulceration is secondary and not usually mistaken for peptic ulcer, and (2) the penetrating or ulcerocancer, which is difficult to distinguish from the penetrating gastric ulcer.

Do Gastric Ulcers Become Malignant?

The histologic evidence of such conversion is too scanty to permit the assumption that gastric ulcer per se is a common precancerous lesion. There are few bona-fide cases in the experience of most surgeons and pathologists — just enough to admit of this possibility. The engrossing and practical question here is not concerned with the possibilities of secondary malignant degeneration of a chronic gastric ulcer (estimate, 5 per cent), but rather whether the ulcerating lesion in the stomach of a given patient is benign or malignant.

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*See Test Your Word Score Page 763.

Age of the Patient

In patients more than 60 years old, one should suspect carcinoma more frequently than benign gastric ulcer. The percentage of ulcerating lesions that are malignant increases with age. Benign gastric ulcer is 15 to 20 times more common in the third decade of life than the ulcerating carcinoma. Comfort and Butsch of the Mayo Clinic found the relative incidence of benign gastric ulcer to be somewhat greater than that of ulcerating carcinoma in all decades except the eighth, but in the eighth decade ulcerating carcinoma was about twice as frequent as benign gastric ulcer.

Size of the Ulcer

Larger ulcers are more likely to be malignant than smaller ones, yet the very small ulcers are sometimes carcinomatous and the very large ones can be benign. Mandred Comfort has presented statistical evidence supporting his contention that the size of the ulcer does have statistical significance.

Location of the Ulcer

Ulcers on the greater curvature of the stomach are almost always malignant. There are occasional exceptions in which some on the greater curvature are benign; on the other hand, there are very few ulcerative lesions, of any type, situated on the greater curvature.

The higher up on the lesser curvature one goes toward the cardia, the higher is the proportion of malignant ulcers. The region of the incisura angularis is the most frequent site of benign ulcers. Holmes and Hampton, of Boston, many years ago stated that three fourths of the ulcers within one inch of the pylorus were malignant. Now it is believed that the incidence of ulcer and of ulcerocancer is about fifty-fifty in the immediate prepyloric region. On the lesser curvature, either benign ulcers or ulcerocancers can occur freely, so that one would never be safe in guessing the nature of any lesion along the lesser curvature no matter where it is, except, perhaps, in the region of the fundus.

Significance of Initial Hemorrhage

The incidence of massive hemorrhage is only about 6 per cent in patients with gastric cancer. Reports on hemorrhage from gastric ulcer relate a frequency of 20 to 40 per cent, or three to seven times as great as that noted among patients with gastric carcinoma.

Significance of Gastric Analysis

In distinguishing between the gastric ulcer that is benign and that in which carcinoma is found, one tends to diagnose benign ulcer in the presence of a higher gastric acidity. The volume concentration and output of acid in the nocturnal gastric secretions are lower in patients with gastric carcinoma than in normal healthy individuals, or in patients having either duodenal or benign gastric ulcer. Nevertheless, there are some carcinomatous ulcers associated with hyperchlorhydria, just as there are occasional benign ulcers accompanied by achlorhydria. One proper conclusion about this relationship is that any patient with achlorhydria and an ulcerating lesion in the stomach should be considered a candidate for surgery, because the odds are at least seven to one that he has gastric cancer (S.M. Jordan).

A review of patients for achlorhydria by Hitchcock, Sullivan, and Wangensteen yielded 1,747 patients with achlorhydria, of whom 19 were discovered to have gastric carcinoma; nine of these (47 per cent) were found to have metastases to regional lymph nodes at the time of operation. These cancers produced no symptoms.

Radiographic Comparisons of Benign Ulcer and Ulcerocancer

Certain possible sources of error in the X-ray diagnosis of benign gastric ulcer and ulcerocancer are (1) hypertrophy of the prepyloric muscle, (2) exaggeration of the mucosal folds with gastritis, and (3) obliteration of the mucosal folds in such a fashion that mucosal destruction by carcinoma is simulated. The margins of the ulcerocancer are usually nodular and irregular, whereas the margins of the benign ulcer are commonly symmetrical, clean-cut, and overhanging. In cancer the crater is within the lumen of the stomach; in benign ulcer it projects beyond the lumen. In ulcerating cancer, the mucosal folds may point to the crater but they do not reach it, terminating at a more or less broad, circumferential plateau of infiltrating cancer. Some of the ulcerocancers have a triangular shape. The more rigid the adjacent wall, the more likely it is that carcinoma rather than benign ulcer is present.

The typical ulcer of carcinoma is usually shallow and saucerlike with the width greater than the depth; per contra, the ratio of the depth to the width of the crater is commonly greater in benign ulcers. The ulcer floor in cancer may be nodular, whereas in benign ulcer it is usually smooth. At times, a fluid level may be demonstrated in the crater of the benign ulcer when the patient is erect, a detail that is not elicited in the case of ulcerocancer. The so-called meniscus sign was considered by Carman and Kirklin as the one sign that almost insured malignancy. Ross Golden has stated that the meniscus sign is produced by a crater in a mass; when pressure is applied, the mass pushes the barium away and leaves barium in the crater with a clear halo around it. Schumacher and Hampton have described a wide band of translucency owing to the overlying margins of the benign ulcer.

Roentgen-ray evidence of healing or diminution in the size of the lesion does not assure its benignancy, because carcinomatous ulcers can become smaller under conservative medical care, but they do not heal completely. The X-ray examination of the stomach under medical management of a supposedly benign ulcer must be repeated until complete disappearance is demonstrated, and there must not be residual rigidity in the gastric wall at the site of the previous ulcer. If the ulcer does not diminish in size under conservative medical care, this should be taken as strong evidence in favor of cancer, and surgical intervention should be recommended.

Gastroscopic Differentiation of Benign and Malignant Ulcers

A benign gastric ulcer usually appears through the gastroscopic ocular as having a clean base and smooth, sharp sides, sometimes with overhanging margins, whereas the malignant ulcer is commonly characterized by a necrotic or hemorrhagic base with irregular margins.

Excised "Benign" Ulcers Found to be Cancerous on Microscopic Study

What percentage of excised gastric ulcers, supposedly benign, are found to be cancerous on microscopic study? This chance of error is surprisingly uniform even in the experience of excellent diagnostic clinics (Table 4). Bille and Rømcke observed that cancer is missed three times as often in patients above 50 years of age as in those below this age, and that the incidence of misdiagnosed cases increases progressively with advancing years so far as males are concerned.

TABLE 4
"Benign" Gastric Ulcers Found to be Cancerous

Arthur Allen (Boston)	14.0%
Samuel F. Marshall (Lahey Clinic)	15.8%
Lampert, Waugh, Dockerty (Mayo Clinic)	13.0%
Ravdin and Horn (99 patients)	11.0%
Tien-Yu Lin (Taiwan Univ. Hosp.: 85 cases)	14.1%
Bille and Romcke (Norway: 908 cases)	2.9%

Therapeutic Tests

The response of the ulcer to a therapeutic trial of medical care is of aid in the differential diagnosis of ulcer from ulcerocancer. However, such management should be done with the patient in the hospital and with the understanding that if the ulcer does not heal and the healing is not progressive and complete, surgical excision is mandatory. Admittedly, ulcerocancer may be mistaken for gastric ulcer, but this error can be safely corrected if the patient is not continued unwisely on medical therapy for a time sufficient to be termed a dangerous delay.

Surgical Treatment of Gastric Ulcer

The patient with a small ulceration in the stomach, in our series of private patients, was considered to have gastric cancer until proved otherwise. In the Memorial Cancer Center, surgical treatment was recommended (by G.T.P.) to every patient with the exception of the following: (1) the youthful subject, under 35 years old, because the chance of cancer was less; (2) the aged subject, more than 70 years old, because of increased operative risk; (3) the debilitated subject, for any reason; (4) the patient with some other disease, the potentialities of which were as serious as the possibility of cancer; (5) the patient who refused surgery.

The ulcer should be removed so that its identity may be established by microscopic study. About 15 per cent of this group of patients are treated medically because of the previously mentioned contraindications to surgery; 70 per cent will undergo subtotal gastrectomy, and a few (5 per cent), total gastrectomy, usually because of an erroneous gross surgical diagnosis of cancer. The resectability rate for ulcerocancer varies from 90 to 95 per cent, with a mortality rate of 7 per cent. The absolute five-year survival rate for patients with carcinomatous ulcer averages 40 per cent. Thirty per cent of patients with gastric cancer who survived five years or longer at the Buffalo General Hospital had cancer which developed in a chronic peptic ulcer (Lipp and Phillips).

An operative mortality of 7 per cent, compared with the hazard of ulcerocancer existing in 29 per cent of patients preoperatively considered to have benign gastric ulcers, would fortify the opinion that the operation is less dangerous than medical treatment. Other surgeons are less inclined to adopt routine surgical therapy. Samuel F. Marshall, for example, contends that only 50 per cent of chronic gastric ulcers require operation. Finally, the reported experience of Welch and Burke may be cited: Of 367 patients with apparently benign gastric ulcers seen at the Massachusetts General Hospital during the years 1952 through 1957, 221 (60.2 per cent) underwent surgery, with a mortality of 3.6 per cent. The postoperative mortality in 47 patients with acute massive hemorrhage or severe grades of anemia was 10.6 per cent, and in the 174 without hemorrhage, 1.7 per cent. Of these patients, 16 (7.2 per cent) had cancer.

The Surgical Treatment of Gastric Cancer

Radical Subtotal Gastrectomy

This procedure remains the standard operation for the treatment of the majority of gastric cancers confined to the distal segment of the stomach. Carcinomas of the antrum or of the posterior wall of the pars media, and the small, ulcerating lesions of the lower lesser curvature are readily resectable by this operation, always in combination with perigastric lymph node dissection and omentectomy.

The salient features of the radical subtotal gastrectomy for carcinoma of the distal gastric segment are as follows:

1. Dissection of all fat, areolar tissue, and lymphoid tissue from the hepatic triad and portal fissure proximally, to include the entire gastrohepatic omentum.
2. Dissection of the gastrocolic and great omenta.
3. Ligation and severance of the right gastric and right gastroepiploic blood vessels.
4. Low transection of the duodenum.
5. Ligation of the left gastric artery at its origin with the celiac axis and dissection of the lymph nodes in the celiac group.
6. High proximal resection of the stomach.
7. Distal pancreatectomy and splenectomy for those cancers of the distal segment that extend appreciably into the pars media, especially along the lesser curvature.
8. Restoration of gastrointestinal continuity by gastroduodenostomy or by gastrojejunostomy.

For the restoration of gastrointestinal continuity after subtotal gastrectomy, the Billroth II principle of repair is preferred over the Billroth I plan of anastomosis.

Transthoracic Esophagogastrectomy

A transthoracic esophagogastrectomy is the generally accepted procedure of choice for cancers of the proximal third of the stomach. The employment of the laparothoracotomy incision and the adequate exposure it affords have produced a dramatic change in the operability of cancers of the proximal gastric segment during the past two decades.

The Extended Total Gastrectomy for Cancer

Total gastrectomy alone is not an adequate operation for cancers requiring removal of the entire stomach, as it does not remove the field of lymphatic spread with the stomach. The extended total gastrectomy based on the anatomic studies of lymphatic spread is the procedure advocated by the authors. It implies complete gastrectomy, partial distal pancreatectomy, splenectomy, dissection of the gastrocolic and gastrohepatic omenta as well as the areolar and lymphatic tissues extending over the hepatic triad to the portal fissure, and clearing of the celiac axis.

Indications for total gastrectomy include: (1) the average carcinomas of the proximal and middle thirds of the stomach, owing to the distribution of the lymphatic spread; (2) carcinomas of such a size and location that they cannot be completely removed by subtotal resection of either the distal or proximal segments of the stomach; (3) carcinomas of the diffusely invasive type; (4) linitis plastica (cancer); (5) all superficial spreading mucosal cancers; (6) carcinomas of the distal segment invading high along the lesser curvature or into the pars media.

Methods of Restoring Gastrointestinal Continuity after Total Gastrectomy. These include:

1. Esophagoduodenostomy (direct)
2. Jejunal interposition between esophagus and duodenum
   a. Method of Longmire and Beal
   b. Method of Claude J. Hunt
3. Esophagojejunostomy
   a. Simple terminolateral anastomosis of the esophagus to jejunal loop either with or without a Braun supplementary enteroenterostomy
   b. Roux en-Y anastomosis
   c. Method of Day and Cunha
   d. Method of Lima-Basto
4. Interposition of transverse colon between esophagus and duodenum
5. Interposition of ilecolon (right) between esophagus and duodenum

Operability and Resectability: Operative Mortality

Lippo and Phillips, in a total of 12,728 patients (18 series) with gastric cancer culled from the literature between 1947 and 1955, reported an operability rate of 70.5 per cent and a resectability rate of 34 per cent; the operative mortality was 15 per cent. An operability rate of 82 per cent and a resectability rate of 49 per cent were reported from the Charity Hospital in New Orleans by Lumpkin, Crow, Hernandez, and Cohn. Of a series of 1,623 patients observed in 1931 through 1955 at the Memorial Hospital, New York City, 1,315 (81 per cent) were submitted to some form of operation; 197 patients (15 per cent) died in the hospital as a direct result of surgery (McNeer, Lawrence, Ashley, and Pack).

A progressive improvement in operability and resectability with increase in age from 30 to 80 years is usually observed. The resectability rate is approximately the same for both sexes.

Prognosis and End Results

Duration of Life in Untreated Gastric Cancer

For the average patient with cancer of the stomach, death occurs within less than one year from the onset of the first symptom or sign, when no treatment is employed. The remaining fragment of life for the average patient, from the time of hospital admission until death is less than four months. As a general rule, all patients with untreated gastric cancer are dead within one and a half years from the time of hospital admission, and not over 3 per cent of these are alive at the end of a year after seeking institutional care.

Operable but Incurable Patients

For those patients who undergo exploratory operations and are found to be incurable, the outlook is much the same as for patients with inoperable cancer, unless the local tumor is resected. Unusual are two patients reported by Lipp and Phillips from the literature who, on exploratory laparotomy, were declared inoperable and who survived five years. Palliative gastric resection may account for prolongation of life in some patients. Patients subjected to nonresectional operations (bypass operations) have survival rates very similar to those of the groups who are inoperable.

Gastrectomy for palliation, as reported from Denmark by Zacho and Fischermann, is seldom, if ever, indicated. A higher mortality occurs, and the accomplishments seldom warrant the procedure. Hoerr and Hodgman aptly state that the best results from palliative gastrectomy occur when the surgeon believes he is performing an operation for cure. Conversely, 22 of 47 patients who survived five years in the Charity Hospital of New Orleans series had what the operating surgeons believed were palliative resections.

Patients Who Have Curative Operations

About 25 per cent of these patients will be alive at five years and of these, approximately 10 per cent will succumb from their cancer after the five-year mark (McNeer, Lawrence, Ashley, and Pack). Most of the therapeutic failures occur within the first three or four years following curative resection. A large proportion of patients who have undergone curative resection for gastric cancer may, therefore, anticipate cure if they have survived this period. The five-year yardstick for the estimation of "cure" would seem to be a practical measurement in assessing the end results for gastric cancer.

Factors Influencing the Prognosis

Various factors influence the prognosis: (1) The symptomatology. Patients with the ulcer syndrome have the highest percentage of cures. (2) The location of the cancer. Patients whose cancers are located in the distal segment of the stomach are cured more frequently than those with tumors in the proximal segment. (3) The gross characteristics of the tumor. Polypoid and ulcerating cancers have a higher cure rate (approximately 45 per cent) than infiltrating cancers (10 to 15 per cent). (4) The degree of differentiation. Grade I cancers have a five-year cure rate of 66 per cent; Grade II, of 40 per cent; Grade III, of 24 per cent; Grade IV, of 12 per cent. (5) Metastasis to lymph nodes. Twelve to 15 per cent of patients with metastasis to lymph nodes proved microscopically are cured in contrast to 40 per cent of those who have no evidence of lymph node metastasis.

To date, surgery has been the only means of curing or controlling gastric carcinoma. Radiation therapy and chemotherapy, as surgical adjuncts and as palliative agents, have been disappointing. Approximately 20 per cent of patients have demonstrated some palliation from megavoltage irradiation but no significantly increased longevity.

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8-30 May be secured from the author or the reprints.

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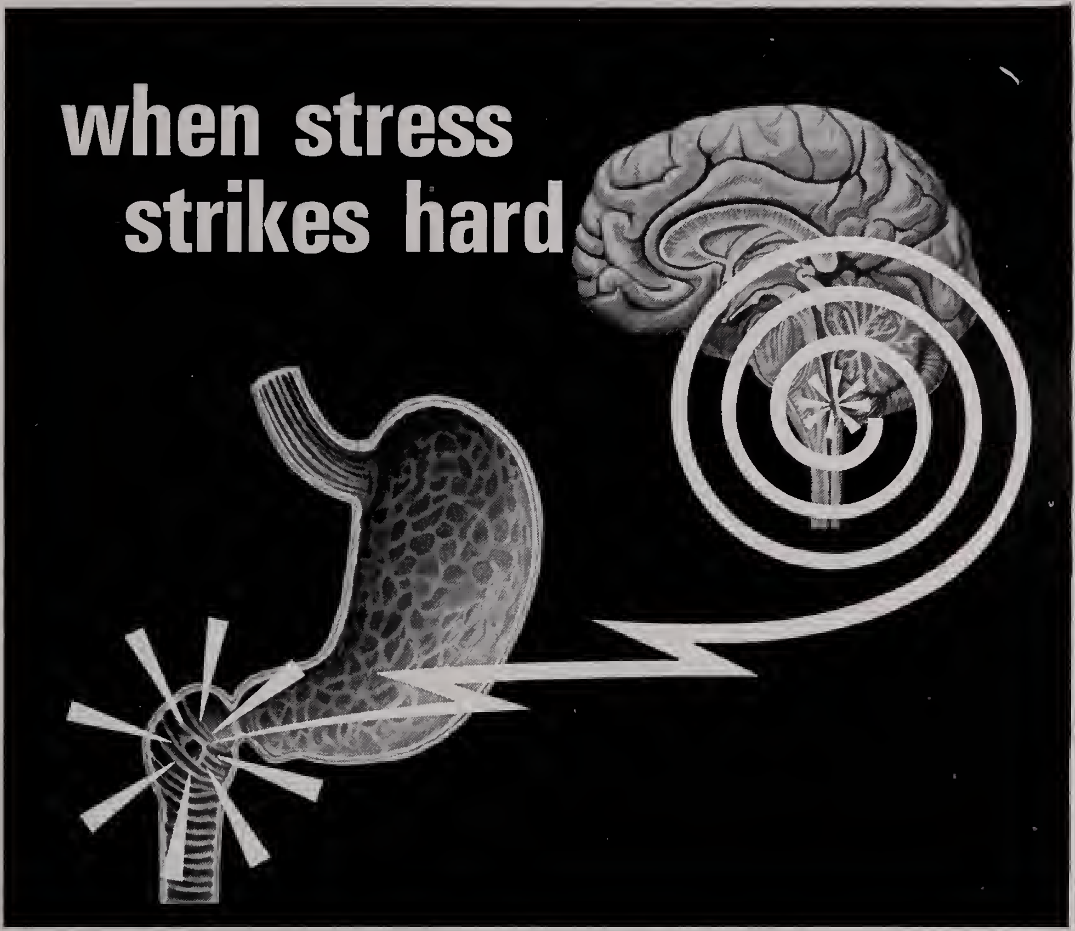
Retirement without the love of letters is a living burial. — Seneca



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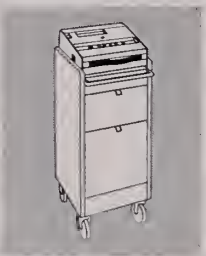

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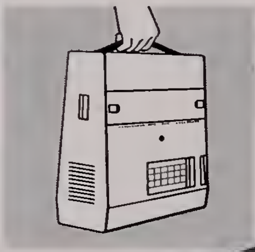

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Editorials

Prevention of Potassium Wasting

Potassium deficiency occurs commonly, and, for that portion of it secondary to diuretic therapy, the physician accepts responsibility. Elsewhere in this issue Snively* reviews concisely the matter of potassium "defect," including its prevention during thiazide therapy with a daily supplement of potassium. The logic, of course, is that renal wasting of potassium, inherent in the action of all thiazides, is the cause of the potassium deficit. Deficits of potassium secondary to thiazide therapy, however, are also accompanied by deficits of chloride and hydrogen ions, and this triad cannot be entirely prevented or completely repaired by potassium salts.

The studies of Sandoe and Olesen[1] illustrate the problems involved in the prevention of potassium deficiency during chronic thiazide therapy. During one month of thiazide therapy, patients in congestive heart failure regularly had hypokalemia (39 per cent of 18 patients), metabolic alkalosis (50 per cent), and hypochloremia (77 per cent). Renal losses were responsible, and balance studies defined the magnitude of the deficits. Prevention of these losses proved to be difficult and incomplete by the daily use of 3 Gm. (43 mEq.) potassium chloride or 400 mg. spironolactone. When potassium chloride was given, hypokalemia still developed in 11 per cent and alkalosis and hypochloremia in 39 per cent. When spironolactone was given, hypokalemia was not observed, but alkalosis was present in 10 per cent, hypochloremia in 68 per cent, and hyponatremia in 23 per cent.

Combined therapy using potassium and spironolactone has been advocated[2] during thiazide administration for patients with fluid retention due to portal cirrhosis, the nephrotic syndrome, or malignant hypertension.

In these conditions, the production of aldosterone is greatly increased, exaggerating the trend toward deficits of potassium. In congestive heart failure, aldosterone production is not as great, and combined therapy can be reserved for patients with refractory edema. Hyperkalemia with hyponatremia may result from therapy with spironolactone and thiazides.

The prevention of potassium deficiency during diuretic administration may not be a simple matter, and it remains a goal of proper therapy.

James C. Broadbent, M.D.
Rochester, Minnesota

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*Minnesota Med Page 713.

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Special Anatomy of Carpal Tunnel Syndrome

PRESSURE ON the median nerve causing motor and sensory deficit in the hand has been reported to occur most commonly at two levels. Occasionally the nerve becomes compressed as it passes through the two heads of the pronator teres muscle at the elbow. More frequently the compromise is at the wrist where the nerve courses beneath the flexor retinaculum. This produces the so-called "Carpal Tunnel Syndrome," reviewed in the study of Doctors Yamaguchi, Lipscomb and Soule in the January issue.* There are few groups that can marshall 1215 patients with this entity for review.

The anatomy of this lesion is of paramount** importance. Every surgical decompression of the carpal tunnel is a lesson in this anatomy. Carpal tunnel syndrome is primarily a problem of disproportion. The rigid walled canal is too small, or its contents too large to allow their comfortable passage. The structure which bellows its distress most vehemently is the median nerve. It is a median neuropathy which usually brings the patient to the physician. Seldom do the other contents of the canal become symptomatic.

The canal itself is an inflexible passageway. Dorsally it is bounded by the concave arch of the eight carpal bones, which are in turn covered by the radiocarpal, intercarpal and carpometacarpal ligaments. The volar roof of the canal is the transverse carpal ligament (flexor retinaculum). This ligament is firmly attached to four bony prominences, the pisiform and hook of the hamate on the ulnar aspect of the wrist, and the tuberosity of the scaphoid and the crest of the greater multangular radially. Ten structures of importance pass through the carpal tunnel to the hand. They include the four flexor digitorum profundus tendons, the four flexor digitorum sublimis tendons, the tendon of the flexor pollicis longus and the median nerve. Symptomatic compression of the latter causes the paresthesias, pain, atrophy and weakness so typical of this syndrome.

The wrist flexors, the radial and ulnar arteries and the ulnar nerve do not pass through the carpal tunnel. The radial portion of the flexor retinaculum splits into two layers to provide a separate compartment for the flexor carpi radialis tendon. Likewise on the opposite side of the wrist the ulnar nerve and artery pass superficial to the transverse carpal ligament through their own tunnel, the canal of Guyon. None of these structures are involved in carpal tunnel syndrome.

The symptoms of carpal tunnel syndrome usually subside in a most gratifying manner when the compression is surgically relieved.

Michael W. Davis, M.D.
Minneapolis, Minnesota

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*Yamaguchi, D. M., Lipscomb, P. R., and Soule, E. H.: Carpal Tunnel Syndrome. Minnesota Med 48:22, 1965.

**See Test Your Word Score Page 763.

Radiological Evaluation of the Hypertensive Patient

RENOVASCULAR CAUSES with curable lesions are conservatively estimated to be present in 2 to 5% of all cases with hypertension. The prevalence of hypertension in the community today is so extensive that a meager percentage represents approximately 5% of the adult population in the United States. Persistent diastolic hypertension, progressive or untreated in the majority of instances, shortens the life span of the victims. Since hypertension of renal origin may be correctable by the use of contemporary surgical technique, whether by vascular reconstruction or nephrectomy, it is essential to evaluate hypertensive patients with currently available diagnostic procedures.

Numerous special diagnostic procedures and observations on "routine" examinations have been developed over recent years. Much experience and sophistication has followed in performing and interpreting intravenous

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pyelography, arteriography, split renal function studies, and radioisotope techniques.

Arteriography is necessary prior to surgery to observe the number and position of the renal arteries. This procedure remains the single most direct means for exclusion of a possibly significant renal artery lesion. A "significant" narrowing does not necessarily mean that surgically "curable" renovascular hypertension exists. In fact, a narrowed artery is not an uncommon finding in our cases that have aortograms for various other reasons. A number of patients have been operated on at the University of Minnesota Hospitals with 50 to 70% narrowing as estimated on angiograms and subsequently confirmed at surgery without relief of hypertension or its symptoms.

Considerable strides have been made in the evaluation of the data obtained from the radioactive renogram. The introduction of Hippuran® has increased the usefulness of this screening procedure greatly. Although in the classical case a fairly typical pattern of unilateral renovascular disease has emerged, there still remains a considerable number of renograms that are nonspecifically abnormal. Additional studies are required for evaluation in these cases. Rarely is the renogram completely normal in the presence of a significant lesion.

Characteristic changes observed on "routine" intravenous pyelography in the past have been infrequently observed in the curable cases. Differences in nephrographic phase and kidney size are poorly appreciated except in the severe cases. Possibly, the measurement of kidney perimeters as recommended by Eelkema in a recent issue of Minnesota Medicine* may improve the percentages.

A recent modification in the intravenous pyelogram, namely, the introduction of a large bolus with rapid sequence films, has remarkably improved the study as a screening agent. Disparity in the nephrogram becomes more evident, and additional parameters such as time of appearance, relative concentration, and clearance of dye from the upper collecting systems are made available. The use of various diuretic agents has further increased the number of diagnosed cases.

Surgically-amenable, renovascular hypertension has been discovered in the old as well as the young. Some patients have had hypertension of long standing prior to diagnosis and have improved remarkably following surgical intervention.

Emphasis therefore must be placed on full evaluation of any hypertensive patient for curable causes, despite age or duration of disease process. What should this evaluation entail? Currently at the University of Minnesota and with slight modification at the Minneapolis Veterans Administration Hospital, the patient referred to the Radiology Department for intravenous pyelography because of "hypertension" undergoes the following studies. A renogram is performed in the dehydrated state, followed by intravenous pyelography employing a combined fast injection and urea-washout technique.

When combined with renogram, the modified intravenous pyelogram will provide an adequate screening test in the majority of cases to determine where further more elaborate techniques, such as split renal function test and/or renal arteriography, are indicated. Much remains to be learned about the factors leading to renovascular hypertension with the basic understanding that it is not always dependent on renal ischemia but may be on the basis of pressure-flow differences between the aorta and the renovascular bed.

E. Gedgaudas, M.D.[**]
Edward Staab, M.D.[†]
Minneapolis, Minnesota

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*Andreassen, Rolf: Renovascular Hypertension. Minnesota Med 48:463, 1965.

**Department of Radiology, University of Minnesota Hospitals.

†Department of Radiology, Veterans Administration Hospital.

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Test Your Word Score

Watch for the asterisks in the manuscripts each month and test your word sense!

Hypokalemia — low serum potassium. (page 714)

Gynatresia — occlusion of some portion of the female genital tract, and used by Merckel to indicate a rudimentary uterine horn filled with menstrual blood. (page 728)

Orthostatic — caused by standing erect. (page 734)

Azotemia — the presence of urea or other nitrogenous products in the blood. (page 734)

Absolutely mandatory — redundant, but forceful expression of double mandate. (page 739)

Eponyms — one whose name is so prominently connected as to be a figurative designation. (page 748)

Exophytic — outward growing — disease originating in some cause lying outside the organism. (page 749)

Paramount — superior to all others. (page 759)

Stele — a slab. (page 825)

Diorite — a granular, crystalline, igneous rock. (page 825)

Shekels — ancient weight and money unit of Babylonia. (page 825)

Letter to the Editor:

I thought you might be interested in an incident which occurred Sunday at the meeting of the Policy Committee of the United States Chamber of Commerce. I have been a member of the Policy Committee for the past four years and have now taken my place as a member of the Board of Directors of the Chamber.

The doctors were well represented, especially by a group from Illinois, and they presented such a strong case against compulsory inclusion under Social Security, that I supported them in the Committee. However, the Committee concluded that Social Security was primarily a tax that should apply to everyone.

I still think it is inequitable for doctors who retire at an average age of seventy-two and would receive so little benefit from their contributions. The other members felt that Social Security is inequitable for lots of other people, so that doctors were included in the Policy Declaration, with only my vote in the negative.

Walter L. Rice
Vice President, Reynolds Metals

Editor's Note: It's been a long tussle, but I guess we have lost. It is interesting to know, however, paradoxical though it may be, that there is one businessman and 207,000 doctors who still believe that the economical security of the people depends on the labor and savings of individuals; that the State cannot be the entity by which everyone lives at the expense of everyone else without exerting one's self.*

P.S. Incidentally that businessman happens to be the editor's brother.

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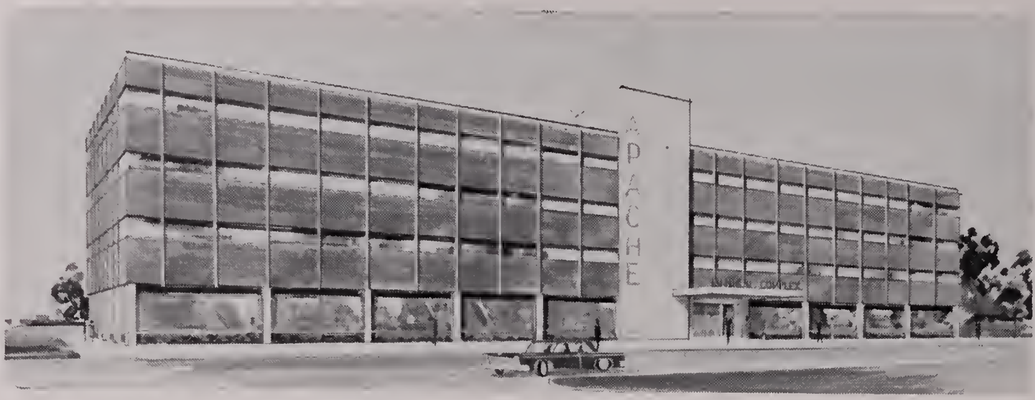
*Statement on behalf of the American Medical Association to the Policy Committee of the Chamber of Commerce of the United States, Washington, D. C., April 25, 1965. Dr. Newton Du Pay, Quincy, Illinois.



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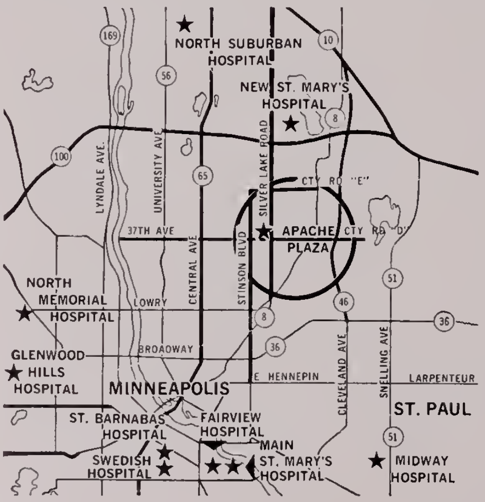
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The Editor's Soliloquy

Your Physiologic Age

The 50 Club

In the natural order of events, life proceeds uniformly from birth to death over an anticipated span of 71 years, a chronological period which cannot be greatly altered on the earth's surface. Astronaut scientists speculate that life processes can be slowed up almost immeasurably if man can be made to glide rapidly through space at the speed of light. Thus propelled, the physiological organism would presumably function so differently that human flesh, blood, and bone could survive for thousands of chronological years without aging more than a few physiologic years, but who among us wants to stay youthful that way?

Everywhere around us we see men and women old, worn, and exhausted at 40; less often we see men and women of 60 with young eyes, young bodies, and young voices belying their chronological age. Some men anticipate the indolence and apathy of retirement at 50; others decline to be put on the shelf at 65. Such are the members of our 50 Club.

A look at the lives of those who are physiologically older than their chronological age usually reveals a pattern of bad habits and excesses; ungoverned dissipation, undisciplined exertion, uncontrolled emotions. In such individuals the complex organism with its intricate balance is forced beyond its capacity to adjust. The body rebels and health abdicates. Cumulative deterioration results; old age sets in; senility arrives prematurely.

The end result is all too apparent on all economic levels, from Skid Row with its derelicts to the more affluent, bourgeois members of the Jersey Cow Key Club, on up to the elected and select habitues of the exclusive Country Club. Retribution does not operate on a caste system.

One of the greatest contributions of the ancient to the modern world was the Greek ideal of moderation in all things. In championing the virtues of maturity, Rostand* has pointed out that "if we leave on one side the great achievement and the splendid discoveries we owe to old men, we must ignore those precious and quiet irreplaceable accumulations of wisdom, doubt, and incredulity that Time lays down in the spirits of those who have been proved worthy to survive to venerable old age."

You physiologically young members of the 50 Club have been wise. You have observed nature's laws and are now in the enviable position of enjoying compound interest on your wise health investment. Salutations!

Carl O. Rice, M.D.

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*Rostand, Jean and Bodin, Paul: Life, the Great Adventure, Charles Scribner's Sons, New York, 1955.

Plato Speaking for Socrates

For death is either to cease from sensations altogether as in a dreamless sleep, and that is no loss; or else it is a passing to another place where all the dead are — the heroes, the poets, the wise men of old. How priceless were it to hold converse with them!

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*Chupkovich, V.; Finnerty, F. A., Jr., and Kakaviatos, N.: The value of chlorthalidone plus reserpine in moderately severe and severe hypertension: A two year study. Presented at the 7th Inter-American Congress of Cardiology, Montreal, June 14–19, 1964.

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Fifty Years of Honorable Service in Minnesota

The presentation of certificates and pins to Minnesota physicians who have engaged in the practice of medicine for 50 years has become an impressive highlight of each Annual Meeting. According to custom the presentations are made during the course of the Annual Banquet. Few who have witnessed these ceremonies soon forget the setting of such an occasion at which these colleagues with a half century of medical practice to their credit so alertly respond to the roll call.

The custom of honoring Minnesota physicians who have served their patients and communities for a half century was established in 1942. Forty-one physicians were honored at the first ceremony. This group also included those who have passed the 50-year mark prior to 1942.

To be eligible for this award a doctor must have spent the majority of his 50 years practicing medicine in Minnesota.

In 1965 eighteen doctors were added to the membership rolls of the Fifty Year Club.

Arthur I. Arneson, M.D.

Dr. Arneson was born on February 7, 1892, to Axel and Brita Arneson, on a farm near Emmons, Minnesota. After his preliminary education, he entered the State University of Iowa, from which he graduated.

In 1917, he served in the United States Army Medical Reserve Corps, thereafter entering general practice in Morris, Minnesota until 1960.

He then took some special training in anesthesiology and since 1960 has limited his practice to anesthesia in the local hospitals in Minnewaska and Starbuck, where he works each morning. In the afternoon he carries on a practice of limited ophthalmology.

Dr. Arneson was an expert rifleman at the University of Iowa Rifle Team and has continued this hobby throughout his life. In addition, he is an enthusiastic fisherman, photographer, lapidarist, and during many of his holidays he searches for semiprecious stones. He is a conservationist and an active participant in outdoor recreation.

He is a member of the local Board of Education and a Director of the Lakeland Mental Health Center at Fergus Falls.

Dr. Arneson married Karine Emmons in 1916 and they have two daughters, both of whom have entered the medical profession as nurses. He has eight grandchildren. Like many physicians, Dr. Arneson has found it impossible to retire from the active practice of medicine.

Dr. Buie, Sr., M.D., A.B., D.Sc., Member Emeritus of the staff of the Mayo Clinic and of the faculty of the University of Minnesota; Diplomate of the American Board of Surgery; member of the House of Delegates of the American Medical Association, 1941 to 1955; member of A.M.A. Judicial Council, 1945 to 1960; Chairman of A.M.A. Council on Constitution and Bylaws, 1951 to 1957. While Chairman of this Council, he was largely responsible for writing the present *Principles of Medical Ethics* of the American Medical Association.

Dr. Buie came to Rochester, Minnesota, February 1917, as a Fellow in Surgery of the Mayo Foundation.

In 1919 he was appointed a member of the staff of the Mayo Clinic. At the suggestion of Dr. W. J. Mayo he organized the Section of Proctology at the Mayo Clinic and served as head of that section from 1919 until 1953, when he became senior consultant. He is Professor Emeritus in the Mayo Foundation Graduate School, University of Minnesota.

Louis A. Buie, Sr., M.D.

Dr. Buie was one of the founders of the American Board of Proctology in 1934, which he also served as secretary and president. He was certified by the American Board of Surgery in 1944. He served as president of the American Proctologic Society in 1927 and 1928 and again in 1934 and 1935. He was president of the Minnesota State Medical Association in 1947 and chairman of the Section on Gastroenterology and Proctology of the A.M.A. in 1947. He was president of the Zumbro Valley Medical Society in 1943 and 1944. He was a member and vice-chairman of the General Advisory Council of the National Foundation for Infantile Paralysis from 1949 to 1960. In July 1955 he was appointed a national consultant to the Surgeon General of the United States Air Force.

Currently Dr. Buie is Secretary-Treasurer of the Advisory Board for Medical Specialties and has served in this capacity since 1958. He has been Editor of *Diseases of the Colon & Rectum* since 1957. He is the author of several books and numerous original articles on diseases of the colon and rectum.

He is a Fellow of the American College of Surgeons and a member of Phi Beta Kappa, Society of Sigma Xi, and Nu Sigma Nu medical fraternity. In 1934 the Government of Italy conferred on Dr. Buie the Cross of Military Merit, and in 1949 the University of South Carolina awarded him the honorary degree of Doctor of Science.

Harry B. Clark, M.D.

Dr. Clark was born in St. Cloud in 1890 and for most of his active years in medical practice has carried on his profession in that city.

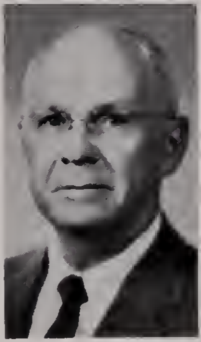
He attended Carleton College, after which he entered the University of Minnesota School of Medicine and spent his internship at the University Hospitals. He was married to Mabel E. Lundgren.

For a short period of time he carried on a practice in Clear Lake, Minnesota, but most of his time has been spent in St. Cloud.

He is on the staff of the Veterans Administration Hospital. He has served on the St. Cloud school board for eighteen years and is a director for the State College Board. He also served in the capacity of president of the State School Board Association.

He has two sons and three grandchildren, who are always eager to listen to his fascinating experiences. He carries on an active general practice.

Dr. Clark served in the First World War, the Second World War and the Korean War as a Medical Officer.



Lloyd T. Davis, M.D.

Dr. Davis is one among a long list of medical doctors. In his home town he is known as Dr. Tom, the youngest son of Dr. A. M. Davis, who has been mentioned in the early history of Wright County as a physician in Howard Lake and who, after practicing a total of fifty years in several localities, died in 1923.

Dr. Lloyd Thomas Davis came to Wadena in 1916 and practiced with his oldest brother, Dr. Luther A. Davis, until 1917, when he entered the United States Army Medical Corps in the first World War and served with the American Expeditionary Force in France. After his brother Luther died in 1920, Dr. Tom was joined by his next older brother, Thayer C. Davis, and the partnership continued until Dr. Thayer's death in 1949.

In 1940, a nephew, Luther F. Davis, joined the group, and in 1946 a son was added to the group, and they practiced together in Wadena until 1954.

Another son, Dr. William G. Davis, has practiced in Hawaii for seven years but is presently a resident in urology in Denver.

Dr. Davis was married in 1918 to Phyllis Dower of Wadena. In addition to the two doctor sons, as mentioned above, they had a son, Michael, a daughter, Denise (Mrs. A. W. Ferron), and a daughter, Judith (Mrs. H. W. Oehler).

Dr. Davis removes himself from the vigors of Minnesota winters, but he returns to Wadena in the middle of April, serving his community largely in the capacity of consultant.

Frank J. Elias, M.D.

Dr. Elias was born on July 1, 1892, in Racine, Wisconsin, where he spent his early days.

He entered Marquette University School of Medicine and graduated with an M.D. degree in 1914. He served his internship in the St. Mary's Hospital in Duluth and thereafter was associated with W. H. Magie, M.D.

In the First World War, he was with the American Expeditionary Force and also served in the British Expeditionary Force.

Dr. Elias, in addition to being a member of the local and state societies, is a Fellow of the American College of Surgeons and served as president of the Minnesota State Medical Society in 1950. He was also president of the St. Louis County Medical Society and one of the Minnesota delegates to the American Medical Association.

He belongs to the Rotary Club and the Royal Order of Jesters, and he was in a partnership group of the Morgan Park Medical Center in Duluth from 1919 to the present date. He was a surgeon with U. S. Steel and the Oliver Iron Mining Company of Duluth.

In 1954 he received the Distinguished Service Medal for his numerous contributions to the welfare of our state medical organization.

He was Chief of Staff of St. Mary's Hospital and president of the Interurban Medical Society in Duluth. His hobbies are greenhouse projects and tape recording.

Continued

Frederick W. Franchere, M.D

Dr. Franchere was born on October 24, 1889, in Lake Crystal, Minnesota, from a third generation Blue Earth County resident. After attending the local schools, he entered the University of Minnesota for two years, then transferred to Marquette University Medical School and graduated in June 1915. He passed State Board examinations in Wisconsin and served a six-month internship in the Milwaukee Children's Free Hospital and a six-month internship in the Lying In Hospital in Chicago.

He then returned to Minnesota and passed the Minnesota State Board examination in 1916. Thereafter he entered the private practice of medicine in Lake Crystal, but at the time of the first World War he joined the American Expeditionary Force and served as a first lieutenant in the Medical Corps in France.

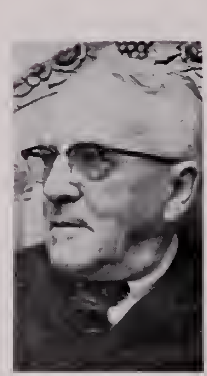
Upon his return he continued to practice in Lake Crystal up to the present date.

He was married to Amanda Larson, a coed at the University of Minnesota, on August 6, 1919. They have two daughters, Mrs. Nilla Franchere Osten of St. Paul, and Helena Franchere Slind of Mt. Prospect, Illinois.

Dr. Franchere is a member of the Zion Lutheran church, Masonic Lodge, American Legion, the Blue Earth County Medical Society and the Minnesota State Medical Society. He is a life member of the International Postgraduate Medical Assembly.

Dr. Halloran was born in Farmon, North Dakota, on August 4, 1889, the son of F. J. and Nell Tracy Halloran. Dr. Halloran's parents were of pioneer Minnesota families. His father practiced medicine in Chatfield and St. Paul for many years.

Dr. Halloran attended Central High School in St. Paul and graduated from St. Thomas College in 1910. He graduated from the University of Minnesota Medical School in 1915 and served his internship at St. Joseph's Hospital in St. Paul during the years 1915-1916. After completion of his internship he was surgical assistant to Dr. W. C. Carroll until the time of his entry into the army during the first World War. While in the army he served at Base Hospital #71 in France.



Walter H. Halloran, M.D.

Upon his return from service he located in Jackson, Minnesota, and was associated with Dr. W. C. Portmann of that city. Together with his father he built and maintained the Halloran Hospital in Jackson for approximately thirty-five years, until it was sold.

In 1920 he married Tereas Ryan, R.N., of St. Paul. Doctor and Mrs. Halloran presently have seven living children. Father Walter Halloran, S.J., a teacher at Marquette University; Mrs. William Harrington, the wife of Dr. William Harrington, Professor of Medicine at Miami Medical School; Dr. William R. Halloran of Milwaukee, Wisconsin; John I. Halloran, a lawyer in Jackson, Minnesota; Mark J. Halloran, M.D., a postgraduate student at Barnes Hospital, St. Louis; Sister M. Gilberte, O.P., a teacher in Chicago, and Mrs. Loren Vorlicky, the wife of Dr. Loren Vorlicky of Oakland, California.

For several years Dr. Halloran has been a member of the Board of Directors of Minnesota Blue Shield and is presently serving as its Secretary.

At the present time, Dr. and Mrs. Halloran maintain the Julie Billiart home for severely mentally and physically handicapped infants in Jackson.

Dr. Hansen was born in Minneapolis on May 22, 1890, and he attended grade and high schools in Minneapolis, after which he entered the University of Minnesota and received his Bachelor of Science degree, followed by his M.D. degree in 1915.

During the First World War, Dr. Hansen served as a Medical Officer with the first division of the United States Army, and at the close of the war he entered the Army of Occupation as it moved into Germany. He received the Croix de Guerre from the French Army and the Silver Star for the United States Army.

Dr. Hansen has been a member of the usual medical societies and was President of the Hennepin County Medical Society, the Minneapolis Academy of Medicine, the Minnesota Academy of Ophthalmology and Otolaryngology, as well as of the American Academy of Ophthalmology and Otolaryngology. He was chairman of the Section on Ophthalmology of the American Medical Association, a delegate from Minnesota to the American Medical Association House of Delegates, and also on the Board of Governors of the American College of Surgeons.

He was a member of the University faculty for thirty-nine years, retiring as Professor and Head of the Department of Ophthalmology in 1958.

Erling Wilhelm Hansen, M.D.

Dr. Hansen was born March 18, 1890, in Hecla, Brown County, South Dakota of Danish homesteader parents. After high school, she went to the Northern Normal and Industrial School in Aberdeen, South Dakota, and later entered the University of Minnesota. In 1913 she graduated with a bachelor of science degree and in 1915 received her doctor of medicine degree. Dr. Hansen served her internship in the University of Minnesota Hospital.

In 1916 she became associated with Doctors S. Marx White and John Sajoie in the practice of medicine in Minneapolis. Dr. Hansen was also an instructor in medicine from 1917-1927 at the University of Minnesota. She joined the Nicollet Clinic in 1921 and is still practicing internal medicine there.

She was married in 1934 to the late Dr. Jennings C. Litzenberg.

Olga S. Hansen, M.D.

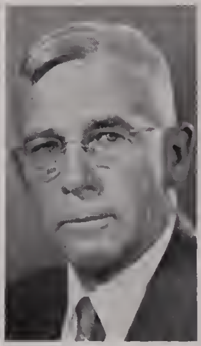
Dr. Havens, a plastic surgeon of the Mayo Clinic from 1928 to 1955, was born on January 22, 1890, at Hallville, Illinois.

In 1912 he received the degree of bachelor of science from Drake University, and in 1915 that of doctor of medicine from the Rush Medical College of the University of Chicago. He served as an intern in Saint Luke's Hospital in Chicago in 1915, and entered the private practice of medicine in Winona, Michigan, in 1916. In 1919 he removed to Waupun, Wisconsin.

Dr. Havens came to Rochester, Minnesota, on April 1, 1926, as a fellow in otolaryngology of the Mayo Foundation. On October 1 of that year he was appointed a first assistant in laryngology, and on April 1, 1928, he was appointed a member of the staff of the Mayo Clinic as a consultant in the Section of Otolaryngology, Oral and Plastic Surgery. From 1929 to 1934 he was an instructor in laryngology in the Mayo Foundation, Graduate School, University of Minnesota; and in 1934 he was advanced to assistant professor. From 1941 to the time of his retirement on April 1, 1955, he was an associate professor.

In 1956 Dr. and Mrs. Havens removed to Riverside, California.

Dr. Havens became widely known in the field of plastic surgery as a result of certain procedures which he either introduced or modified to enhance their usefulness.


Fred Z. Havens, M.D.

Dr. Havens was certified as a specialist in otolaryngology and plastic surgery. He was a member of the American Academy of Ophthalmology and Otolaryngology, the American Association of Oral and Plastic Surgery, the American Laryngological, Rhinological and Otological Society, the American Medical Association, the American Laryngological Association, the American Society of Plastic and Reconstructive Surgery, the Minnesota Academy of Ophthalmology and Otolaryngology, the Minnesota State Medical Association, and the Alumni Association of the Mayo Foundation.

Continued

Reuben A. Johnson, M.D.

Dr. Johnson was born July 30, 1889 in Colton, California. He attended public school at the South High School, Minneapolis and graduated from the University of Minnesota Medical School in 1915. He did postgraduate study in Vienna, London and Berlin and completed his internship at Abbott Hospital in Minneapolis.

He served as a first lieutenant in World War I, and after the war began his practice of medicine in Minneapolis.

Dr. Johnson was associated at one time with Dr. William E. Petersen and served on the Abbott, Mount Sinai and St. Barnabas hospital staffs. He was a clinical professor of medicine at the University of Minnesota and a diplomate of the American Board of Internal Medicine.

In the past, Dr. Johnson has served as first vice president and chairman of the Board of Censors of the Hennepin County Medical Society and was a former first president of the Minneapolis Society of Internal Medicine. He also was a past secretary and treasurer and past president of the Minnesota Society of Internal Medicine.

He was married to Gladys Sievers, now deceased, and they had three children. Dr. Johnson presently is spending his retirement in Minneapolis.

Herman O. McPheeters, M.D.

Dr. McPheeters, F.A.C.S., F.I.C.S., F.A.C.A., was born January 31, 1891, in Mankato, Minnesota. His family then moved to Aitkin, Minnesota, where he was graduated from the Aitkin High School in June 1909. Thereafter he received his premedical education in Hamline University and then transferred to Northwestern Medical School where he acquired his M.D. degree in June, 1915.

He served his internship at Wesley Memorial Hospital, after which he entered the Army and served for a year in the First World War.

In 1919 he became associated with N. H. Schelderup, M.D., who was a general surgeon, and remained with him until 1924, when he independently entered into general practice and surgery. After 1935, he limited his work to vascular surgery and continued as one of the outstanding authorities on the treatment of varicose veins. In this capacity he did a considerable amount of research work and developed some of the principles that are still used in the treatment of varicose veins, stasis, ulcers and vascular problems of the extremities. Many of his original ideas still remain the basis upon which numerous vascular problems are solved.

He was licensed in both the states of Illinois and Minnesota in 1917.

He married Ethel T. Anderson of Redwood Falls, Minnesota; they have one son, George Edward, and a daughter, Mary Ann (Mrs. Looe Baker, Jr.).

Dr. McPheeters is now retired from active practice; but he does some consultation work and remains constantly active in his numerous hobbies.

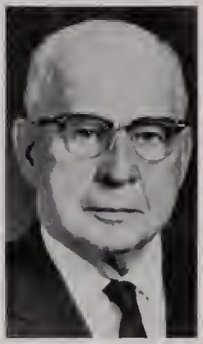
Frank B. Mach, M.D.

Dr. Mach was born in New Prague, Minnesota in 1891. He entered the University of Minnesota Medical School in 1909 and graduated in 1915. After completing an internship at Minneapolis General Hospital, he started practice in Northeast Minneapolis, where he has remained ever since. At the present time, he has his son, Dr. John R., practicing with him.

During the first World War, Dr. Mach entered the United States Army Medical Corps as a Captain and was attached to the Royal Army Medical Corps in the European Theater, where he obtained valuable experience and contributed a much needed service to his country. He then returned to Minneapolis and has been affiliated with the staff at St. Mary's Hospital since 1916.

He was married to Alice Neary in 1924. They have two sons, Robert F. and Dr. John R., and one daughter, Mrs. Mary Clifford Peterson.

Dr. Mach enjoys an active general practice and in his spare time he amuses himself with gardening and other hobbies. He has not missed a Minnesota home football game in fifty-six years.



Fredolph H. Magney, M.D.

Dr. Magney was born on March 4, 1886, in Trenton Township, Pierce County, Wisconsin. He attended public school in Bayport, Minnesota and graduated from Amery High School in Wisconsin.

He then became interested in pharmacy and attended the Minnesota Institute of Pharmacy, becoming a registered pharmacist in 1908, after which he practiced pharmacy in Duluth and Minneapolis for a few years.

This activity in pharmacy apparently stimulated Dr. Magney's interest in medicine and he then entered Gustavus Adolphus College for some additional academic work and transferred to the University of Minnesota, finally receiving his medical degree in 1915. He served his internship at the City and County Hospital in St. Paul. After his internship, he entered the Army Medical Corps as a regimental surgeon with the 125th Field Artillery, serving with the American Expeditionary Force in France as a Captain.

After his return to the United States, he entered practice in Duluth in 1916, and continued to remain in active practice in the field of surgery until 1962.

He has a long list of achievements, having been President of the St. Louis County Tuberculosis and Health Association and Chief of Staff at St. Luke's, St. Mary's and Miller Hospitals. He has also been Chief of the Surgical Section at St. Luke's and Miller Hospital and has been Chief of the Obstetric Section of these hospitals.

Dr. Magney has fulfilled the responsibility of numerous civic duties and has proven his sterling qualities by serving as President of the Duluth Chapter of the Professional Men's Club of America, the St. Louis County Tuberculosis and Health Association and the Duluth Surgical Society. He has been a Director of the Duluth Chamber of Commerce and the Duluth Chapter of the American Red Cross.

For thirty years he served on the Minnesota State Board of Medical Examiners. He is a member of the Rotary Club, the Pilgrim Congregational Church, the T. W. Hugo A. M. & A. F. Lodge, the Scottish Rite, the Duluth York Rite and the Aad Temple. He was President of the Hay Fever Club of America. He was justifiably awarded the Distinguished Service Medal by the Minnesota State Medical Association and he was also awarded the Silver Beaver by the Boy Scouts of America. He was married to Ruth Taylor in 1922, and they have four sons, Roy Taylor, Robert Gorham, Paul Herman and Mark Jonas.

Though Dr. Magney still maintains interest in medical organizations and serves as a consultant on numerous occasions, he is enjoying a well deserved semi-retirement.

Morton P. Morse, M.D.

Dr. Morse was born and went to school in LeRoy, Minnesota, which is a little town near Rochester.

He entered the University of Illinois in Chicago and graduated with an M.D. degree in 1915. This same year he was licensed to practice medicine in Iowa. He served his internship in what is now the Hennepin County General Hospital.

During World War One, he served as Captain in the Medical Corps of the United States Army.

Since 1917, Dr. Morse has been in practice in LeRoy, Minnesota.

Continued

Edgar R. Sather, M.D.

Dr. Sather was born at Willmar, Minnesota, in April, 1889.

He attended the University of Minnesota for his premedical training and then the University of Iowa at Iowa City, where he received his medical degree in 1915. He interned at the Minneapolis General Hospital.

He practiced at Spring Valley, Minnesota, from 1916 to 1922, with two years out for Service in the British Army. In December 1922, he moved to Alexandria, Minnesota, and has practiced there ever since. In August 1919, he was married to Ragna Molstad of Spring Valley, Minnesota. They had two children, Mrs. James Swenson of Alexandria, and Rev. Edgar Sather, who is at present teaching in Anatolia College in Thesseloniki, Greece.

Dr. Sather has been president of the Park Region Medical Society, a delegate to the Minnesota State Medical Society, and first vice president of the State Society. He has also been President of the Park Region Section of the Ameican Academy of General Practice. In 1931 he was president of the Alexandria Kiwanis Club and the next year was Commander of the American Legion Club 87 of Alexandria. In 1955 he was moderator of the Central division of the Congregational Church and the next year was named moderator of his home church.

He has been Chief of Staff of both Douglas County and Our Lady of Mercy Hospitals in Alexandria. He is a member of the Indigent Doctors Committee and has been a member of that committee since its inception.

Dr. Sather is still in active practice.

Charles W. Waas, M.D.

Dr. Waas was born in Pittsburgh, Pennsylvania, on December 1, 1888. The major portion of his medical education was acquired in Canada, where he attended St. John's College in Winnipeg and graduated from the University of Manitoba cum laude in 1915. He obtained his license to practice from the Medical Council of Canada in June, 1915, after which he served his internship in the Winnipeg General Hospital.

He entered the practice of general medicine in North Dakota, where he remained for five years, when he transferred to St. Paul, where he has conducted his practice up to the present date. He is a member of the Ramsey County Medical Society, the Minnesota State Medical Society, the American Medical Association and the American Association of General Practitioners.

Clayton K. Williams, M.D.

Dr. Williams was born in Minneapolis on February 2, 1891. He received his Bachelor of Science degree from the University of Minnesota in 1914 and his M.D. degree the following year. He served his internship at St. Joseph's Hospital and began practice in St. Paul in 1916, where he has remained.

His practice was limited to internal medicine. During the Frst World War he served as Captain in the United States Army Medical Corps.

He was married to Natalie C. Carter in 1919.

He was Secretary of the Ramsey County Medical Society from 1944 to 1946 and President of that Sociey in 1948. In addition to belonging to the usual county, state and national medical societies, he is a member of the Minnesota Academy of Medicine.

Curbstone Consultation

Muscular Problem Among Alcoholics

QUESTION: In a recent discussion among a group of colleagues one of them stated he had the impression some type of muscular syndrome was occasionally associated with chronic alcholism. I am aware of the neuropathies that may accompany alcoholism but have never heard of an associated muscular problem among alcoholics. Do you have knowledge of such a condition?

ANSWER: There has recently been described both an acute and a chronic muscular syndrome associated with marked alcoholic abuse. In the acute syndrome patients present with muscular aching, tenderness, and edema. Some have associated renal damage with hyperpotassemia. Extensive necrosis of muscle fibers can often be demonstrated on pathological examination. The chronic variety apparently manifests itself in one of two ways. In one group there may develop gradually a symmetrical weakness of the proximal limb and girdle muscles without evidences of an acute process. In the other group there are no symptoms of muscle disease, but electromyography and biopsy can demonstrate changes.

Muscular strength apparently returns following cessation of drinking and institution of proper medical care.

Transhepatic Cholangiography

QUESTION: Would you do transhepatic cholangiography if you did not plan to do a laporatomy?

ANSWER: I would not do percutaneous transhepatic cholangiography unless I planned to do a laparotomy. However, if I found a normal biliary ductal system, removing the possibility of obstructive jaundice, I would not proceed with operation, since it would be contra-indicated. We have had patients with long-standing complete obstructive jaundice, particularly those with carcinoma of the pancreas with metastases, who have not tolerated the procedure well and in whom we have inserted a small polyethylene tube and proceeded to allow the ductal system to be decompressed by this method.

Frank Glenn, M.D.
Cornell University Medical College

We do not know what to do with this short life, yet we want another which will be eternal. — Anatole France

Striking the right

NOTE

'Actidil', one of the most potent of antihistamines, strikes the right note in the treatment of allergies.

As in the case of other antihistaminic agents, excessive dosage may produce drowsiness. Patients should be advised to postpone potentially hazardous activities requiring mental alertness until the optimum dosage level has been determined.

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Fracture–Trauma Conference

Fat Embolism and Pelvic Fracture

Management of the patient who has sustained a fractured pelvis entails preparedness on the part of the physician to treat the associated injuries (i.e. extremity, head, thoracic, abdominal) which occur so frequently in the type of accident which produces pelvic fractures. He must also be alert to the presence of continuing retroperitoneal hemorrhage from the fracture site which may in itself cause death by exsanguination. Another complication is fat embolism. This may occur with any fracture and, in fact, has been described in instances where no fracture was detected.[1]

In the following case history in spite of a rather minimal displacement of the pubic rami at the fracture site and no clinical evidence of other significant injury the patient's hospital course was complicated by fat embolism which very nearly proved to be fatal.

Case History

An 81-year-old male pedestrian was struck by a slow moving automobile on the afternoon of 12/7/62. He was admitted to Swedish Hospital where x-rays (iFgure 1) revealed fractures of the left superior and inferior pubic rami with minimal displacement of the fracture fragments. An old degenerative arthritis of the left femoral head was also detected. He was well oriented and in good general condition for his age. He was put to bed and closely observed.

The following morning the patient was doing well, bright and alert, until at 1:30 P.M. or approximately 18 hours following injury, he became incontinent of urine and noted some slight difficulty in breathing. That evening he seemed obtunded and failing to eat, he was given an intravenous solution of 5% dextrose and water. During the night his condition deteriorated and by 8:00 A.M. 12/9/62 he was in acute respiratory distress and comatose. An emergency tracheostomy was performed, which afforded him considerable relief. At this time petechiae were found to be present over his chest and upper arms. A diagnosis of fat embolism was made and confirmed by the finding of free fat on urine examination.

He was slightly improved on 12/10/62 and nasogastric tube feedings were initiated. On 12/12/62 he was able to take food orally and the tube feedings were discontinued During the patient's hospital stay his hemoglobin fell from 12.9 gms % to 9.7 gms. %. However, on discharge it had risen to 12 gms %. Gradual improvement continued until at the time of his discharge to a nursing home on 1/2/63 it was apparent that he had entirely recovered his mental faculties and he had no difficulty with respiration following removal of his tracheostomy tube.

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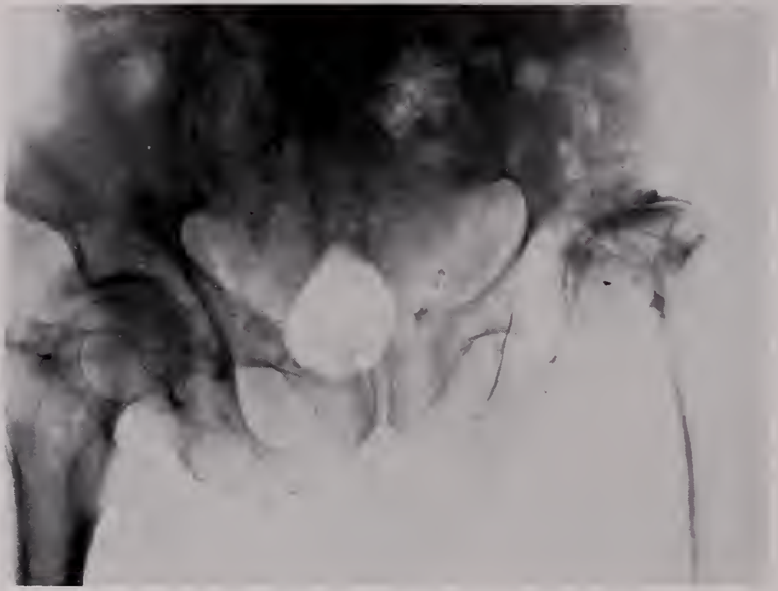

Fig. 1 — X-ray demonstrating fracture of left superior and inferior pubic rami.

Discussion

How often does fat embolism occur in cases of trauma? Is it produced by the entry of bone marrow fat or local fat into the general circulation or is it a result of a rather precipitous change in the lipid content of the blood?

These questions continue to provoke different answers from different authors with different supporting bits of evidence.[2-5] Nevertheless, there is no question but that, as in the case presented, fat embolism may occur after what would otherwise appear to be a rather minimal injury as well as with more severe trauma. For this reason any patient with an injury severe enough to require hospitalization should be closely observed.

Signs

A change in the patient's mental awareness, the development of dyspnea, the appearance of petechiae over the chest, upper arms and conjuctivae, and fever are objective signs that may be observed in patients with fat embolism. An unexplained sudden drop in the serum hemoglobin level may be related. The pulmonary symptoms are usually the first to be manifested.

Tests

Sputum and urine samples may be stained with Sudan III and if present the doubly refractile fat can readily be seen under the microscope. It is possible to biopsy the petechiae to prove the diagnosis. In stained sections of pathological specimens the fat appears as in Figure 2.

Treatment

Intravenous solutions of fat solvents have been recommended but in general, the results from their use have been disappointing. In the recent past, steroids have been tried and the results have been encouraging. Further data on their use is needed before recommendation for general

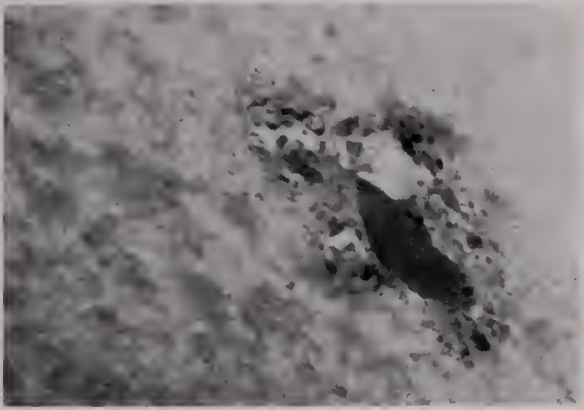

Fig. 2. — Photo micrograph of fat emboli in brain tissue.

use can be made. The use of intravenous heparin with its well known lipolytic effect has been recommended; however, to use such an agent in the early hours following a fracture, especially one in which massive bleeding may go undetected, would seem to be unduly dangerous.

The physician and hospital staff can provide good supportive care which includes intravenous or nasogastric fluids, an adequate airway with proper respiratory tract toilet, careful management of an indwelling urinary catheter, and good nursing care. Many of these patients will clear their vascular system and tissues of the offending emboli if they can be successfully tided over the first few critical hours by judicious medical management.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

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Medicine Comes of Age

By mid-nineteenth century Medicine, in one respect, no longer trailed behind the Church and the Law. On January 25, 1856, The (London) Times wrote: ‘Of the three learned professions, the medical has attained the highest character for disinterestedness. Hard things are said of the cupidity of the clergy, the wealth of certain benefices affording a strange contrast to the poverty of the primative Church; still harder things are said of the lawyers, who are supposed to eat the contested oyster while the plaintiff gets one shell and the defendant the other; but there is probably no class of the community generally so free from mercenary motives as the members of the medical and surgical profession.’*

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*Turner, E. S.: Call the Doctor. St. Martin's Press Inc., New York, 1959.

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M.M.

Tumor Conference

Synovial Sarcoma, Lower Extremity

A 16-year-old otherwise healthy male presented a history of noticing a lump in the upper outer area of the left thigh at the region of the great trochanter. He has no recollection of bruise or injury. Over a four-month period the mass gradually increased in size and was painless. A somewhat ill-defined soft mass presented 5 x 4 cm. No skin or vascular changes were evident on inspection.

Under general anesthesia, a well-encapsulated 8 x 6 cm. mass that easily shelled out was removed by enucleation. There appeared to be an attachment to, or near the capsule of the hip joint. It did not arise from the hip joint itself.

Microscopic examination revealed a typical mixture of sarcomatous-appearing cellular background with scattered areas that appeared glandular in configuration. Diagnosis, therefore: Malignant synovioma synovial sarcoma. The case is presented for recommendation for future therapy.

Discussion and Review

Ackerman[1] describes synovial sarcoma as an intimate intermingling web of adenomatous structures and a sarcomatous-like stroma. Stout[6] suggests that the tumor may arise from embryonic synovioblasts near, but not from, the joint. The origin near the joints is an important differential since synovial hyperplasia, hemangiomata, etc., arise within joint structures.[1]

An early review of 104 cases reported by Haagensen and Stout[4] in 1944 cite only three cases free of tumor in five years. However, a later series reported from New York Memorial Cancer by Pack and Ariel[5] in 1950, present much better figures (absolute 5-year survival of 19.1 per cent, therapeutic 5-year of 23.5 per cent and a 10-year of 16.7 per cent). The difference in the two series appears to be based upon more radical treatment in the Memorial Hospital group. Haagensen and Stout recommended more radical treatment because of the poor results from less aggressive treatment and Pack and Ariel attributed the improvement to employment of more radical methods. This frequently involved amputation.

Pack and Ariel[5] advised that the tumor be approached first by application of a tourniquet above the lesion, then aspiration or very small incisional biopsy, and finally if the biopsy was reported as malignant synovioma, an amputation was done below a second tourniquet — that is, between two tourniquets. The double tourniquet technique is designed to prevent pickup implantation from the biopsy to the amputation site.

Continued

Reports[5,1,3] indicate a better chance for cure in the younger age group. Crocker and Stout[3] suggest a well planned wide local excision in children under 15. Whenever the location is feasible, an amputation may, therefore, be avoided. Regional lymph node dissection is advocated[5,4,6] since this particular sarcoma has an appreciable (16.6 per cent[5]) node involvement.

Recommendations

Since the lesion in this patient is in an unfortunate location, too near the hip joint to permit an adequate wide local excision, and since even a hip disarticulation would fall short of adequate criteria for cure, a hemipelvectomy is the only operation designed to fulfill the requirements of adequate excisional therapy. Such a procedure presupposes a negative chest X ray and absence of evidence of metastases. Furthermore, a sarcoma, particularly of this high grade malignancy, does not, in fact, have any capsule. The apparent encapsulation is tissue compressed by tumor growth and in all likelihood, tumor cells will be found in adjacent tissue. Amputation after recurrence appears has been quite unsuccessful; none in the Haagensen[4] series have achieved 5-year survival.

If surgical treatment is refused, then X-ray therapy should be employed with at least some chance of prolongation of life.[5]

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St. Barnabas-Swedish Hospitals
Minneapolis, Minnesota

Urea Wash-Out Test

The April issue carried an article, "The Urea Wash-out Test," by Dr. Edward V. Staab et al. (pages 448-454). On page 450 under the sub-head "Technique" eight lines down, Dr. Staab has requested that we correct *500 c.c. of 8 per cent saline* to read *500 c.c. of 8 per cent urea in normal saline.*

The Editors

No man ever got nervous prostration pushing his business: You get it only when the business pushes you. — Fra Elbertus

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Though the people support the government the government should not support the people. — Grover Cleveland

Neurological Conference

Retinitis Pigmentosa*

Dr. Robert Soll

Retinitis pigmentosa is a rare condition, whose importance is shared by many other conditions which are similarly rare, that is how readily might it be recognized in a patient? If it is recognized, what treatment, if any, can be employed to improve the condition and what counsel can be given to the patient and his family? These are very crucial questions in this type of case and bear significantly on the patient's future life.

Dr. Alan R. Sinaiko**

The patient is a 16-year-old boy who complains of difficulty in hearing and seeing. Apparently his hearing difficulty has been present since age five. He has been followed at the University Hospital since 1955 and during the past nine years has had four audiograms, which revealed a decreased acuity for higher frequencies. He was given a hearing aid after his initial hospital visit, but unfortunately, because of numerous small problems, he did not wear it consistently.

His visual problems began approximately two years ago when he first noticed a decreased visual acuity at night. One year ago he went to an ophthalmologist and was given glasses for myopia. Within six months he had required stronger glasses because of continued decreasing vision; however, since that time he believes his vision has remained unchanged. For the past year he has virtually complete night blindness.

Family History

His family history is significant in that he has one 12-year-old sister who is deaf, and also a paternal grandmother, great uncle and great aunt who are deaf. There is no definite history of any previous visual difficulty in the family. The patient has had an eighth-grade education marked with numerous difficulties in school, primarily because of inability to hear

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*Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatric conferences are held the first and third Wednesdays of every month from 3:15 to 4:15 p.m. The adult conferences held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Robert W. ten Bensel, in Pediatrics, and Dr. Robert Soll, in Adult Neurology.

Held November 5, 1964.

**Student doctor, University of Minnesota Medical Center.

Continued

and slowness in reading. During the past four months he has been working as a laborer for a construction company.

Examination

His most recent physical examination revealed a definite hearing loss, and on funduscopic examination numerous darkened pigmented patches distributed in a typical "bone spicule" configuration were apparent at the periphery of the retina. The macular area itself was normal. His visual acuity at this time was 20/60 in the right eye and 20/50 in the left eye without glasses; with corrective glasses his central acuity was approximately 20/20 in both eyes; but his peripheral vision was decreased to approximately one half of normal. The remainder of the physical examination including neurological examination was normal.

Dr. John Brantner*

The present psychological tests indicate a border-line performance. These tests were given to him in writing and approximately duplicated the school situation. Since he was handicapped at school by difficulty in reading, these tests may also be inconclusive.

Nonverbal Intelligence Tests

On a nonverbal intelligence test such as the Porteus Mazes he attained an average IQ of 104. His basic abilities would be considered in the average range. You would expect him to handle with ease practical situations such as those in contruction work or even higher-level work, where he would doubtless react normally and not appear defective. The appearance of his disability or handicap would be noted only if he were asked to read or if he tried to use abstract thinking or verbal skills. He does not show in either the Porteus or the Graham Kendall tests, both of which are quite sensitive, any signs of organic brain damage.

He was also given the Minnesota Multiphasic Personality Inventory, but the results were of a random sort. He either did not understand the items, or more likely was unable to read them. The scores on the various scales show that he answered 53% of one of them, 47%, 48%, 49% and so on, approximately a 50% average, and resulting only in the type of profile that can be obtained by shuffling the cards and guessing half of them true and half false: a totally invalid personality test.

So this is a boy who is functioning at a border-line level in verbal skills without showing brain-damage evidence on the tests. He probably has average or slightly above average intellectual skills, but he is handicapped. These results point to further testing that ought to be done, such as a full diagnostic intellectual work-up to identify areas of this handicap in verbal skills, especially since we do have tests that are suited for non-hearing or hard-of-hearing subjects. If he intends to advance further in schooling, I think that he could profit by reading diagnostic tests which would determine exactly which skills of the many that are involved in reading are below normal. Also, we have personality tests that do not require reading; and I think that he ought to be given these. For example, the Rorschach test does not require the ability to read or to write.*

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*Clinical psychologist, University of Minnesota Medical Center.

Dr. Robert Letson*

Retinitis pigmentosa is primarily a selective degeneration of the neuroepithelium of the retina. As it is usually manifested in the equatorial region of the eyes, the pupils should be dilated on examination. Early stages of retinitis may appear before age 10 or during the first decade, although it may appear later. The progression is slow, but usually complete blindness is present by age 50; however, I have seen some patients in their 60s who still have good central vision. There are accumulations of pigment which are spicular in type, often surrounding the retinal vessels; these gradually migrate or progress to involve the entire posterior pole of the eye as well as the peripheral retina. In addition to these black accumulations of spicules or fine bone spicule formation, there is often narrowing of the vasculature of the retina to the point that the vessels almost disappear.

In later stages when the optic nerve has degenerated, optic atrophy is also apparent. There is degeneration of all the layers of the retina, but primarily the rod and cone layer is involved. Macrophages pick up pigment and migrate toward the vessels. Many of them disintegrate, leaving pigment accumulations around the retinal vessels. Often when visual fields are done on these patients, a ring or doughnut-shaped scotoma will be found. This is because the degeneration is rather selective, starting between 15°-30° from the point of central vision, and proceeding both centrally and peripherally, widening the scotoma and eventually involving the macular area.

Clinical Syndrome

The clinical picture is really a syndrome, because many of these individuals often have high myopia, cataracts, and deafness associated with the retinal changes. Occasionally we have to remove the cataracts which have developed, but unfortunately, such removal may not necessarily help the patient's vision, since retinal changes have also occurred. Whether the lens or the retina is the relatively greater factor in causing decreased acuity is difficult to establish. Therefore treatment must be individualized in each case. Frequently we can improve central visual acuity. In a youngster, myopia usually will continue to increase until age 25 or 30.

The Type of Cataract

Usually a cataract does not appear until the fourth or fifth decade as a later manifestation of the disease: an ordinary senile-type cataract, although the patient is really presenile. Both central and peripheral types of cataracts occur; there is not just one specific type such as diabetics develop.

Prognosis

The prognosis is usually unfavorable, because symptoms will definitely progress to eventual blindness. Unfortunately we have no specific treatment as far as the retinal disease is concerned, but as has been mentioned, keeping the refraction up to date and removing the cataract are of value; in this way, patients can be helped for a while. Usually by age 50 their

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*Resident physician, department of ophthalmology, University of Minnesota Medical Center.

Continued

visual function is gone; but some have maintained vision until age 60 or 70.

Differential Diagnosis

The differential diagnosis includes chorioretinitis due to inflammation. This disease, however, causes a focal and sharply demarcated lesion and may be unilateral. The phenothiazine drugs when given in large doses for long periods may cause a similar picture in the fundus, but this entity can be excluded by the history. There are other primary retinal degenerations which may resemble retinitis pigmentosa, but a discussion of these is not of general interest.

Dr. Soll

The counsel that the physician gives to his patient and the patient's family concerning the eventual disability of the patient is very important. Of course, with this young boy, it is very important for him to know that he may be able to function well for many, many years and lead a productive life in spite of the fact that he has trouble with his vision and hearing. It would also be well if we could detect all such children before age 10 so as to at least inform the parents of this possibility before they have other children.

Mrs. Gloria Gross*

The patient has had the same type of hearing loss since he was first seen in 1955. Both pure tone and speech audiometry remain unchanged from previous results. Two ears respond similarly to pure tone. There is no suggestion of middle ear pathology that would require attention. We do find that acuity for the low frequencies is virtually normal but that he has a fairly sharp loss for high frequencies. This means that he can hear the human voice and the vowels almost as well as we can. Without the use of amplification, some of the consonants are only partially audible; therefore, without amplification, this boy can hear speech, but only incompletely and with difficulty.

The Body-worn Hearing Aid

He came into the clinic not wearing his aid, and such a fact is usually significant. The instrument he presently owns is a body-worn type, to be placed underneath his clothing. Both clothing noise and low frequencies are amplified by the instrument.

The Ear-level Hearing Aid

With the ear-level instruments produced today, extraneous noise is greatly reduced. This patient has responded well to the ear-level type of instrument; he is much better able to understand lip-reading. I don't believe that the patient is at all interested in the cosmetic appearance of the hearing aid; I don't think he wants an ear-level instrument just because it looks nicer.

Speech Adversely Affected

The patient's speech has been adversely affected by his hearing loss in that it corresponds to what he hears. Consequently, some consonants are distorted. I would assume that much of the boy's poor progress in school could be attributed to the fact that he was not hearing well. If he were in a classroom without a hearing aid and were not able to lip-read, then he would not know what was being said. A hearing aid is definitely recommended and I am confident that he could learn to use one.

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*Clinical audiologist, University of Minnesota Medical Center.

Dr. Soll: At what frequencies do the consonants occur specifically?

Dr. Frank Lassman:* Consonants such as l, n, b, and r, are subserved by energy approximately in the range of 700 to 800 cycles up to about 3000 cycles. Other consonants such as t, p, k, sh, f, and soft th would be subserved by energy above 1200 cycles to about 3000 cycles. There is energy at other frequencies beyond 3000 cycles in these consonants, but the presence or absence of this energy is not critical to the auditory discrimination of these consonant sounds. The most important range, then, would be from approximately 1000 cycles to 3000 cycles; this is an octave and a half in length, the range in which his hearing is down about 40 to 50 decibels.

Dr. Richard Magraw:** Would there be any difference in the audibility of a man's or woman's voice?

Mrs. Gross: No, not necessarily; the point that I tried to make earlier was that he does hear a voice, and if it is a fairly good voice, then he should be able to discriminate speech fairly well. But he will make errors in differentiating some consonant sounds from others.

Dr. Lassman: If the woman is a soft-spoken individual, it might have some effect on his ability to hear, especially in a noisy background. But Mrs. Gross's point about the precision of articulation is the most critical one.

Mr. Thomas Fawcett†

The only problem this family has ever presented to the county welfare department has been for authorization to help procure his hearing aid. Both parents have visited us several times. The first time I was aware of the patient's visual problems was probably one month ago. The family lives on an 80-acre farm. They are trying to make a living there but it is difficult. Both parents are also working at other pobs. The community probably has not been too sympathetic as far as the patient is concerned. This fact is possibly part of the patient's troubles in school. His father has said that when his son was in the eighth grade, he was doing about straight F work. He would have been better off in the third grade. The whole difficulty according to the father was that the patient couldn't read. Consequently he dropped school and got a construction job, and from all reports, he has done very well. His employer has been very satisfied, although I don't know how long this may last. If his problem is progressive, he may have to get trained for some other type of work. The likelihood that he will do quite well for many years is very good.

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*Professor of speech and audiology, University of Minnesota Medical Center.

**Associate professor of medical psychology and director of Comprehensive Clinic Program, University of Minnesota Medical Center.

†County Welfare department, Gaylord County.

Continued

Mr. Romeyn Clarke:* The boy seems to be a rather likable young fellow. The family is financially marginal and have had a very hard time. The mother, age 34, gives the impression of being a very energetic person who is working hard to make ends meet. The father, age 44, first started farming right after marriage on his own family's farm; but this didn't work out. After five years he had to go out and work in a cheese factory, and now he is working in a manufacturing plant. His take-home pay is not over $70 a week for a family of six. The patient is the second of four children. An older brother, age 17, is now finishing high school; a sister, age 12, also has a hearing problem; another brother, age 10, seems to be doing well. The home is not too well kept up. The mother has to do outside work whenever she can, although she doesn't like to leave the family. She works during the canning season, but when there is a poor crop like this year, she attempts to get another job. She raises a little stock and some grain and does all the work on their little place. They do a large amount of subsistence farming since that is the only way they can get by. Now I presume that she is a fairly permissive mother, not driving the children very hard.

There was a hearing aid problem in that the patient was teased at school. He frequently had to fight and often came home in a bloody state. For this additional reason it has been difficult to make him and his sister wear their hearing aids. The mother finds it very hard to say to the children, "You just have to do this," because she remembers her own experience of being teased when she was young. At this point she feels that she can adjust to the hearing difficulty; but she has also been told that the patient is going to be blind and she doesn't have the heart to talk about it.

Finally, I would like to add that the patient's recent job experience has apparently been very good for him. Wearing a hearing aid which has any kind of cord, as his mother explained to me, interferes with his work; perhaps this inconvenience could be eliminated by an ear-level hearing aid. He is working on a construction job as a helper, carrying bricks up to other workers or helping load concrete. Often he has to be told several times to do things. In general this has been a good experience except that fellow workers who started with him now are getting a raise and he isn't. This is hard for him to take.

Dr. Milton Alter**

The association of retinitis pigmentosa and deafness is known as Usher's syndrome, an entity well described in ophthalmologic literature. Retinitis pigmentosa is actually found in a wide variety of clinical disorders. A survey of Pennsylvania school children who had visual acuity under 20/200 revealed 1.3% with retinitis pigmentosa. Another survey in Switzerland revealed one individual in 7000, or 0.0143%, affected with retinitis pigmentosa.

There are several varieties of hereditary transmission of retinitis pigmentosa that have been reported in different pedigrees. According to Francois, the autosomal recessive variety accounts for about one third of the cases. There is an autosomal dominant variety which accounts for about 20% of the cases; 4% follow a simple recessive form of inheritance. There is also a rare form which is sex-linked. The remainder of the cases were either sporadic or the data was inconclusive to establish the nature of the transmission.

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*Senior social worker, University of Minnesota Medical Center.

**Instructor, department of neurology, University of Minnesota Medical Center.

Autosomal Recessive Trait

If both parents are carriers of an autosomal recessive trait, it is transmitted to ¾ of the offspring on the average, but only ¼ receive a double dose and show the trait. Males and females are affected with equal frequency. See Figure 1.

	R	r
R	RR	Rr
r	Rr	rr

Retinitis pigmentosa is represented as the small r, and normal by the large R.

Fig. 1

The diagram also illustrates that one half of the offspring are asymptomatic carriers and one fourth are normal. If a carrier now mates with another carrier, again one fourth of the offspring would be affected. However, since the trait is rare, a carrier is more likely to marry a normal individual, in which case no offspring would be affected, but one half would be carriers. See Figure 2.

	R	r
R	RR	Rr
R	RR	Rr

Fig. 2

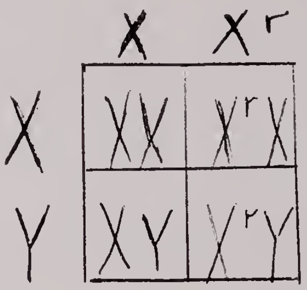
It is readily appreciated that a carrier is more likely to marry another carrier if he mates with a close relative. Hence, the consanguinity rate is high among parents of individuals with rare recessive traits. The more rare the trait, the higher the rate. An average of 26.7% consanguinity has been reported for retinitis pigmentosa, compared to less than 1% in the general population.

Sex-linked Recessive Inheritance

Sex-linked recessive inheritance is more complicated. One half of the male offspring of a carrier female are affected, and one half of the daughters are carriers and can transmit the disorder to their sons. The female contributes one of her two X chromosomes to the zygote. Since only one of her X chromosomes is defective the risk that the disease will be transmitted is 50%. If the defective female X chromosome unites with

Continued

a normal X chromosome contributed by the father, a carrier daughter results. The normal X supplies the genetic information lacking in the defective X chromosome. On the other hand, if the father contributes a Y chromosome which unites with a defective X chromosome, an affected son results. He shows the trait because he has no normal X chromosome to supply the genetic information lacking on the defective X chromosome received from the carrier mother. See Figure 3.



	X	X^r
X	XX	X^rX
Y	XY	X^rY

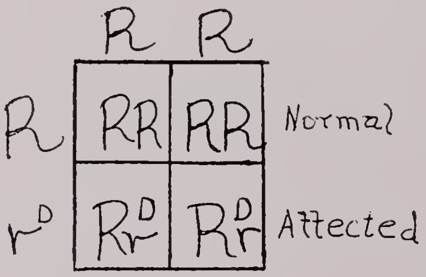
X = normal chromosome
Xr = defective chromosome
Y = male chromosome

Fig. 3

It has recently been shown that only one of the X chromosomes in the female is active in a given cell. The X chromosome which is inactivated is selected at random very early in embryogenesis. On the average, one half of the female's cells are normal and the other half defective. Some slight defect in the carrier female, therefore, would be anticipated and, in the case of retinitis pigmentosa, this has actually been found. Female carriers of retinitis pigmentosa may show some pigmentary degeneration of the retina as well as defective color vision, mainly for blue and green. A scintillating golden reflex from the macula and perimacular area has also been described.

Autosomal-dominant Inheritance

The autosomal dominant form of inheritance is straight-forward. One half of the offspring of an affected individual are also affected in this situation. See Figure 4.



	R	R	
R	RR	RR	Normal
r^D	Rr^D	Rr^D	Affected

r^D = dominant type of retinitis

Fig. 4

Sporadic cases may be new mutations, phenocopies of the genetic disorder, or inheritance from individuals who had the defect but in whom the defect did not penetrate. Penetrance is a useful concept which has perhaps been abused by some geneticists. If an individual shows any stigmata of the trait, the disorder has penetrated; the degree to which it has penetrated is called expression. While penetrance is an all-or-none phenomenon, expression is quantitative.

The Patient's Pedigree

In our patient's pedigree, we are probably dealing with an absence of penetrance. The maternal grandfather had 16 siblings who were entirely normal. The paternal grandmother, however, was deaf and had a deaf brother and sister. One of the patient's siblings was still-born and a 12-year-old sister has some evidence of deafness as well as early signs of retinitis. This appears to be transmission of a dominant trait, and some of the other siblings not yet examined probably also show evidence of the disease. See Figure 5.

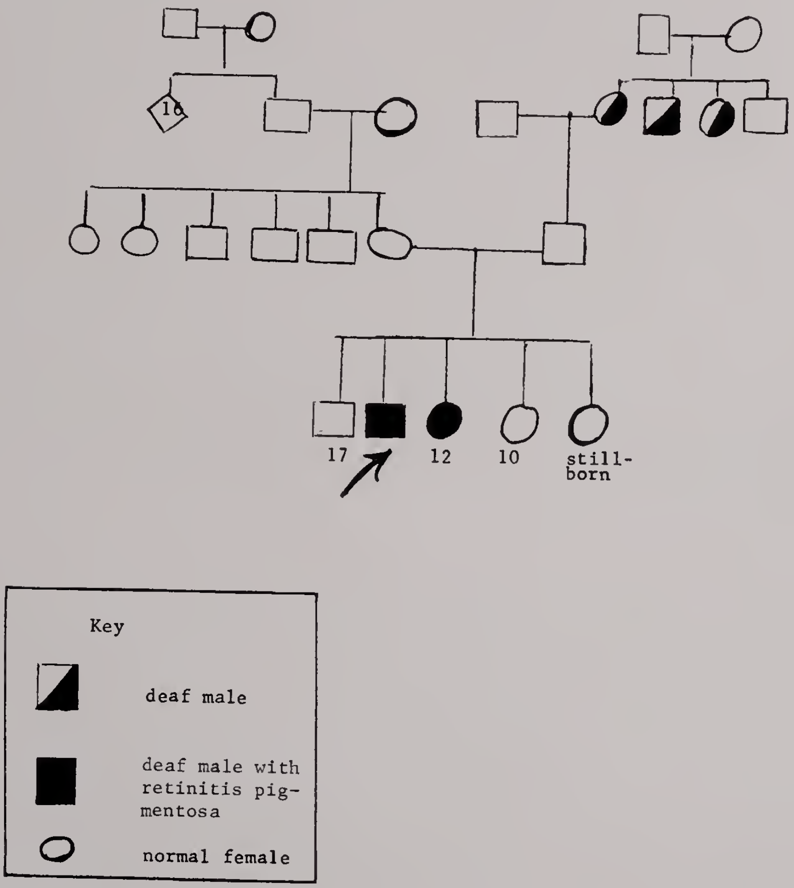


Fig. 5

Agents which can produce retinitis pigmentosa give rise to nonheritable phenocopies. The defect in such cases cannot be transmitted. It has been reported that phenothiazine, thioridazine and ethylphenothiazine can cause retinitis pigmentosa.

Some eye signs associated with the defect include narrow vessels, optic atrophy, decreased color vision and an abnormal electroretinogram. Less often, glaucoma and microphthalmia occur. Retinitis pigmentosa has been

Continued

observed in Laurence-Moon-Biedl syndrome, in Friedrich's ataxia, and occasionally in Marfan's syndrome.

Experimental work of interest includes the observation that about 50% of affected individuals have positive F II latex fixation tests. In some individuals the 19S macroglobulins are increased, suggesting that the disorder is not localized to the retina.

A strain of rats with retinitis pigmentosa has been studied. A decreased ability to carry out anaerobic glycolysis in the retinal cells has been found in them. The defective enzyme was believed to be triose phosphate dehydrogenase. In addition, amino acid abnormalities were discovered. Taurine was increased in affected retinas; glutamic acid was only half the normal value, and aspartic acid was synthetized at 2-4 times the normal rate. The implications of these studies for humans are intriguing, but a relationship has yet to be demonstrated.

It appears that the trait is a dominant one in our patient, and thus we would predict that 50% of the patient's children would be affected. It is unlikely that he would marry an affected individual.

If the father shows neither deafness nor retinitis pigmentosa, he represents a lack of penetrance. However, he must have the defect in order to have transmitted it to the patient and the patient's sister.

Dr. Sinaiko: How do you know that the deafness in this paternal grandmother, aunts and uncles was also due to this gene?

Dr. Alter: That is an educated guess. We don't know for certain because we are lacking information about the father, but we know he has a deaf mother, aunt and uncle. We know the patient is both deaf and has the eye defect. It is convenient to assume that all those affected have the same disease, until proven otherwise.

Dr. Lassman

For many good reasons, some of them historical, this boy has not had the advantages of special educational tutoring and rehabilitative services which are available from both public and private resources in Minnesota today. The physicians present should take note that a hard-of-hearing youngster with related speech problems who has had difficulty learning to read and has had some other associated problems in school has a wealth of resources waiting to assist him. It needs only the physician to properly trigger the mechanism. The Minnesota Legislatures of 1957 and 1958 made it financially possible for a school district to pay the salaries of remedial-reading teachers, speech correctionists, teachers of the hearing-impaired and the slow-learning, etc. They also made it possible for a school district to purchase necessary remedial services and tutoring from adjacent school districts. Later legislation improved opportunities for the transportation of youngsters needing special helps to the source of the help. The law makes the proper education of special children mandatory and not just permissive; i.e., the school district is responsible to "educate" its children or must locate such educational opportunity elsewhere.

Another important development is the establishment of responsibility for special education in a section of the Minnesota Department of Education, called the Division of Special Education. Mr. Ellsworth Stenswick heads this division which includes a hard-working staff who can help interpret the Special Education laws to school boards, superintendents, and principals. In theory, no youngster with a visual and hearing problem having trouble in school need go without assistance. In practice, this sometimes takes some aggressive action by the physician to assist local educational agencies to both recognize their problem (the handicapped child) and to find a solution (state special supports for special tutoring, speech correction, etc.)

There are other special resources developing locally and regionally: the Audiology and Speech Pathology sections of the University Hospital; the College of Education Psycho-Educational Clinic; the Speech Clinics at UMD, Mankato, St. Cloud and Moorhead State Colleges; the speech programs at St. Paul Rehab Center and at the Kenny Institute; the Minneapolis and St. Paul Hearing Societies; and many more. One of the most important and helpful agencies is the Division of Vocational Rehabilitation, Minnesota Department of Education, which will support education, vocational training, and job placement. The State Department of Public Health and Division of Crippled Children's Services, Department of Public Welfare, hold regional speech and hearing clinics. A most interesting recent development is a Speech and Hearing Camp run by the Minnesota Society for Crippled Children, which looks like a useful summer project for the next few years.

Handicapped children need special help as early as possible. The resources are here — now — in Minnesota. It is up to us to help get the two together.

Robert Soll, M.D.
Moderator
University of Minnesota
Medical Center

Participating in the conference: Alan R. Sinaiko, student doctor; Dr. John Brantner, clinical psychologist (University of Minnesota Medical Center); Miss Helen Kretchmer, supervisor and assistant professor of social service (University of Minnesota Medical Center); Dr. Robert Letson, resident physician, department of ophthalmology (University of Minnesota Medical Center); Mrs. Gloria Gross, clinical audiologist (University of Minnesota Medical Center); Dr. Frank Lassman, professor of speech and audiology (University of Minnesota Medical Center); Dr. Richard Magraw, associate professor of medical psychology and director of the comprehensive clinic program (University of Minnesota Medical Center); Mr. Romeyn Clarke, senior social worker(University of Minnesota Medical Center); Mr. Thomas Fawcett, county welfare department, Gaylord County; Dr. Milton Alter, instructor, department of neurology (University of Minnesota Medical Center); and Dr. Robert Soll, chairman, adult community services (University of Minnesota Medical Center).

Subsequent to the conference this patient was given the Rorschach, the Chicago Non-verbal Examination, and the Gates Reading Diagnostic Tests. These showed that his intelligence is in the low average range with considerable deficiency in verbal skills. His judgment, foresight, grasp of abstract concepts and memory are normal. The personality tests do not show any unusual patterns of thought, beyond a mild lack of positive pleasure. Conclusion: low average to average intellectual capacity, normal personality, reading deficit but with ability to benefit from remedial training.

Our greatest glory is not in never falling but in rising every time we fall.
— *Confucius*

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Grand Rounds

Hyperparathyroidism

The incidence of hyperparathyroidism is difficult to estimate but it certainly is not great. However, an understanding of this complex disease is important because it leads to irreversible renal damage, and if recognized early in its course can be cured by surgery. Although the pathologic physiology and anatomic changes in primary hyperparathyroidism are quite well understood, the etiology is not known.

In an analysis of 100 cases at the Massachusetts General Hospital, ages ranged from 12 to 72 years with 80% between three and 60. The female to male ratio was 7:3.

Pathology

From Table 1 it is apparent that the most frequent cause of hyperparathyroidism is parathyroid adenoma, the location of which is as variable as that of the normal glands. The upper parathyroid glands develop from the fourth branchial pouch, usually descend to the level of the cricoid cartilage, and are situated on the posterolateral surface of the lobes of the thyroid gland. Occasionally there is an invagination of the parathyroid gland into the capsule of the thyroid, and in rare cases the parathyroid gland may be located within the body of the thyroid.

The lower parathyroid glands originating from the third branchial pouch are much more erratic in their location, varying from their normal position at the lower border of the thyroid gland to a location in the anterior mediastinum and occasionally behind the esophagus. Approximately 75% of adenomas occur in the lower glands. The number of glands is also variable, ranging from four to 10. With a functioning adenoma, there is usually atrophy of the other glands. However, in 3% of cases multiple parathyroid adenomas may be present.

The mean size of a single human parathyroid gland is approximately 5 x 5 x 3 mm., and the total weight of all four glands is 118 mg. The glands are reddish or yellowish-brown in color with distinct stalks. There are

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Presented as a Medical Grand Rounds at Mt. Sinai Hospital, Minneapolis, July 28, 1964.

Continued

three cell types present: chief cells, which are 6-8 μ in diameter and contain glycogen; the "wasserhelle" or water-clear cell, which is larger and vacuolated; and the oxyphil cell, which contains no glycogen and varies in size from 11 to 14 μ. There is controversy as to whether this cell is associated with any function.

In an adenoma there can be any mixture of these various components. Most of the adenomas are comprised mainly of chief cells; the nuclei of which are usually large, filling about half the cells. In adenomas, cells with two or three nuclei are not uncommon, so that darkly-staining pyknotic nuclei may lead to an incorrect diagnosis of malignancy. Mitosis and anaplasia are not seen in adenomas and are still valid criteria of carcinoma. The cells are usually arranged in broad bands or in the shape of acini in a highly vascular network.

Carcinoma

These tumors are usually functioning. At operation the surgeon may recognize their presence by their adherence to the surrounding tissue. Metastases usually appear first in the regional lymph nodes. Microscopic examination shows no rim of normal parathyroid tissue as may be found in adenomas, capsular invasion, and extension of the capsular connective tissue into the tumor as dense contiguous septa with glandular cells that are larger and more atypical. It is not known whether adenomas may be the origin of carcinomas.

Hyperplasia

The gross appearance is different from that of an adenoma in that the gland is irregular in shape with projections. The glands are soft and a darkish brown. On microscopic examination the capsule is thin and no normal parathyroid tissue can be seen. The only type of cell present is the wasserhelle cell, with variable patterns of arrangement. All the glands are enlarged, rather than atrophic as found in the presence of an adenoma or carcinoma.

Bone Lesions

Extreme decalcification results in poorly formed, very pliable bones,

TABLE I

Types of Parathyroid Gland Pathology in Primary Hyperparathyroidism***

Pathologic Classification		Cases	
		Number	Per cent
Single parathyroid adenoma		343	89.1
Multiple parathyroid adenomas	10 cases		
With polyendocrine adenomas*	10 cases		
Without polyendocrine adenomas	11 cases		
Total cases		21	5.5
Primary parathyroid hypertrophy and hyperplasia**		19	4.9
Parathyroid carcinoma		2	0.5
Total cases		385	100.0

*Multiple parathyroid adenomas associated with tumors of the pancreatic islet cells or of the anterior pituitary gland or of both glands.

**Primary (wasserhelle-cell) parathyroid hyperplasia.

***These data from the Mayo Clinic series were supplied through the courtesy of Dr. B. Marden Black. The tabulation includes all cases up to December 31, 1959.

Williams Endocrinology
3rd Edition, Saunders publ.

resulting in marked deformities, a condition called osteitis fibrosa or von Recklinghausen's disease of bone. The decalcification may be either generalized or localized; in the latter, cysts may be produced. Within the medullary cavity brownish areas may be seen which represent the proliferation of large numbers of osteoclasts. The cysts and decalcification result in weak bones and fractures in severe cases.

Kidney

The specific lesion is the deposition of calcium in the renal tubules and the interstitial tissue, i.e., nephrocalcinosis, resulting in impaired renal function with an increased incidence of pyelonephritis. Renal calculi are very common (Table 2).

TABLE 2
Clinical Features of Urolithiasis in 50 Patients with Functioning Parathyroid Tumors

	No. Patients
Recurrent calculi	25
Bilateral calculi	29
Opaque calculi	50
Single calculus	7
Multiple calculi	33*
Nephrocalcinosis	10

*Staghorn calculi in five patients.

R. J. Veenema
California Medicine
Vol. 95, No. 2

Metastatic Calcification

Deposition of calcium in soft tissues may occur. The kidneys are the most common site, but metastatic calcification may be seen in the lung, stomach, pituitary gland, and in almost any other location.

Calcium and Phosphorus Metabolism

The basic function of the parathyroid glands is the regulation of calcium and phosphate metabolism. The various clinical pictures of hyperparathyroidism are the end result of hyperfunction.

Both calcium and phosphate, although principally found in the skeleton, are, in varying amounts, distributed throughout all the body compartments, and their presence is essential in maintaining several important processes. Among the many roles of calcium are:

1. Participation in formation of bones and teeth (the skeleton containing over 99% of the body calcium).
2. Maintenance of normal blood coagulation by serving as a cofactor in the conversion of prothrombin to thrombin.
3. Regulation of membrane permeability.
4. Maintenance of normal cardiac rhythmicity.
5. Regulation of excitability of nerves and muscles.
6. Maintenance of normal muscular contraction.
7. Maintenance of normal renal tubular concentrating mechanisms, i.e., calcium excess will cause lesions of the distal renal tubules, resulting in a loss of concentrating power.

Continued

8. Maintenance of normal enzyme activity.

9. Normal development of the fetus during pregnancy and of the newborn infant during lactation.

The main site of calcium absorption is the upper small intestine, especially the duodenum. Once calcium has reached the colon it is present as insoluble salts and is not available for absorption. The absorption of calcium is enhanced by several factors; chief among these are D vitamins, parathormone acting in the presence of permissive amounts of vitamin D, and the state of the calcium stores of the body.

In plasma, it is the ionized calcium which is metabolically important, not the total amount. Alkalosis or an increase in phosphate or citrate may result in more bound calcium, while the total amount remains normal. The reverse is true in hypoproteinemia, where the total calcium value may be decreased, but the ionized calcium fraction may be normal.

Ten per cent of the total excretion of calcium is through the kidney, the remaining 90% through the intestinal tract. The major route of phosphate excretion is the kidney rather than the intestine.

For clinical purposes we may express the relationship of the calcium and phosphate ions in the plasma by the relationship, calcium conc. x phosphate conc. equals a constant. A rise in the concentration of either ion will result in a fall of the other.

Actions of Parathormone

On the Kidney

Parathormone causes an increase of renal tubular reabsorption of calcium, and there have been three suggested actions in regard to phosphate and the kidney: parathormone may increase the glomerular filtration of phosphate; increase the tubular reabsorption of phosphate; and increase the tubular secretion of phosphate.

Action on Bone

The direct effect of parathormone appears to be the conversion of cells from osteoblastic to osteolytic activity. This has two consequences: decreased bone formation and increased bone reabsorption, resulting in the simultaneous breakdown of both the matrix and mineral components of bone, and a release of calcium and phosphate ions.

Action on the Gastrointestinal Tract

Parathormone causes an increase in the absorption of calcium from the small intestine. This action seems to occur by the hormone, acting in the presence of permissive amounts of vitamin D improving the concentration gradient across the mucosa.

DeLuca[2] in a study of kidney mitochondria found that vitamin D and parathyroid hormone act synergistically to promote the release of calcium from isolated mitochondria and that the presence of the vitamin is necessary for this action to take place. This in vitro demonstration has been supplemented by the in vivo studies of Rasmussen[3] who demonstrated that administration of 200 to 500 units of bovine parathormone induces severe hyperparathyroidism in the vitamin D-fed rat but has little or no effect upon calcium and phosphate concentration in the vitamin D-deficient animal.

Calcitonin

Recently, evidence has been presented that there probably exists in addition to parathormone, a second active substance, Calcitonin, which acts to lower serum calcium. Copp,[4,5] using an isolated thyroid and thyroid-parathyroid perfusion system, demonstrated that perfusion with high calcium concentration resulted in a fall in serum calcium within a few hours only if the parathyroid glands were part of the perfusion system. This effect was different from that of parathyroidectomy, which resulted in a much longer period of time before the drop in the serum calcium occurred. It has also been shown that this perfusion effect is obliterated by parathyroidectomy[6].

Tests of Parathyroid Function

At present a sensitive and reliable method for measurement of parathormone is not available. Such a test would directly measure parathyroid function. Isotopic-immunologic techniques show promise and may be the answer to this problem.

Serum Calcium

Levels of serum calcium measured by the EDTA chelating technique[7] greater than 10.5 mgm% are definitely abnormal, and suggest the presence of hyperparathyroidism. Calcium measurements by this method are reliable screening tests for parathyroid hyperfunction.

Serum Phosphate

This is characteristically very low in primary hyperparathyroidism in the absence of renal damage. The measurement of serum phosphate is, however, less reliable and more variable than serum calcium.

Serum Alkaline Phosphatase

In cases with significant bone involvement, alkaline phosphatase is elevated. Chiandussi[8] has reported chromatography of the various fractions of serum alkaline phosphatase, but as yet these have no diagnostic advantage. Alkaline phosphatase is an index of bone formation, not parathyroid function.

Ionized Fraction of Calcium

Rose[9] discovered that by adding a small amount of murexide dye to a solution of calcium ion at or near the neutral pH, the subsequent colour intensity was proportional to the calcium ion concentration. This test is of value in borderline cases, especially those associated with abnormal serum proteins, azotemia, or other complicating biochemical features.

Urinary Calcium Excretion

a. Qualitative Sulkowitch Test. Buffered oxalate solution added to urine produces a calcium oxalate precipitate and a cloudy solution. However, the correlation with quantitative calcium measurements is poor and this is an unreliable index of hypercalciuria.

b. Quantitative measurement. The patient is placed on a diet in which the total ingested quantity of calcium per 24-hour period is known. This

Continued

usually is approximately 150 mgm. After three days preparation, the urinary 24-hour calcium excretion is measured. Normally, an amount equal to ingested calcium is excreted in the urine. In primary hyperparathyroidism the urine excretion of calcium exceeds the intake by more than 50 mgm. An excessive excretion of calcium indicates an inability to maintain calcium balance.

Cortisone Test

Two hundred to four hundred mgm. daily of cortisone are given for seven days and the serum calcium determined daily. A fall to normal serum calcium levels indicates secondary hypercalcemia and is against the diagnosis of primary hyperparathyroidism. This test is generally quite reliable, but there are occasional falsely positive or negative results.

Tubular Reabsorption of Phosphate

One of the primary actions of parathormone is to increase the excretion of phosphate by the kidney tubules. The filtered load of phosphate presented to the tubules can be calculated by multiplying the serum phosphate concentration by the creatinine clearance. By calculating the total phosphate excreted, i.e., the urinary phosphate concentration times the volume of urine, the tubular reabsorption ratio of filtered phosphate can then be calculated.

Gordon had found that 43% of his series of surgically proven hyperparathyroidism had TRP values greater than 80%.[10] Low values for tubular reabsorption of phosphate, characteristic of primary hyperparathyroidism, can occur in other hypercalcemic states such as multiple myeloma and sarcoidosis.

Serum Chloride Levels

Wills[11] compared serum chloride levels in primary hyperparathyroidism and those obtained in other disorders associated with hypercalcemia, such as sarcoidosis, hypervitaminosis D, and myelomatosis and found that in hyperparathyroidism there is almost always an elevation of serum chloride above 102 mEq./L., whereas in secondary hypercalcemia the serum chloride is almost always below this level.

Calcium Turnover in Bone

A number of tests have been designed to evaluate the rate of calcium turnover in bone.

a. Intravenous strontium test — devised by Fraser.[12] As the metabolism of strontium is similar to calcium, the rate of skeletal deposition of calcium can be followed with a radioactive tracer dose of strontium. Strontium gluconate is injected intravenously and the concentration of strontium in the urine and plasma is measured for the next six days. From the curves of radioactivity in plasma and urine, the rate of transfer of calcium into bone can be calculated. Two indices are thus obtained: CaE — the exchangeable calcium pool, and CaB — the rate of calcium deposition in bone. The advantages of this test over the one to be described next are that it is more sensitive; a smaller dose of radioactive material is needed; and the radioisotope has a shorter half-life than Ca^{45}.

b. Intravenous radiocalcium infusion test using Ca^{45}. This test is similar to the strontium test except that plasma and urine concentrations must be followed for two weeks. Rich[13] has described a test using a constant intravenous infusion of Ca^{45}, shortening the observation period.

Rapid Calcium Infusion Test

Goldsmith has described a new modified rapid calcium infusion test.[14] Both normal and hyperparathyroid subjects exhibit a progressively increasing phosphaturia between the hours of 8 A.M. and 12 A.M.. By calculating the ratios of phosphate concentration to creatinine concentration in the urine a curve can be constructed. The 9 A.M. value is considered 100% and subsequent ratios expressed in relation to it. A baseline is obtained on the first day; on the second day 180 mg. of calcium is injected intravenously. The curve in normals shows depression after calcium infusion when compared to the baseline curve. The principle underlying the test is that normally elevation of serum calcium results in a depression of parathormone secretion, increased phosphate retention, and decreased urinary excretion of phosphate, which acts to lower the urine phosphate-creatinine ratio. In hyperparathyroidism, there is a lack of response to increased calcium levels and the depression of the curve does not occur. In Boeck's sarcoid a characteristic sawtooth curve is produced by calcium infusion.

Serum Citrate Level

It has been reported that serum citrate levels are elevated in primary hyperparathyroidism.[15] Hodgkinson has demonstrated that while serum citrate is usually elevated, this is closely correlated with serum calcium and is not an indication of bone involvement.[15]

Bone X Rays

Bone surveys by X ray may be used to determine if typical bone changes are present. X rays of the hands, skull, and lamina dura may be particularly helpful.

Kinemometry

With the hypotonicity sometimes present, one may use kinemometry to document the increased contraction and relaxation time of tendon reflexes.

Clinical Manifestations of Primary Hyperparathyroidism

It is almost an understatement to categorize this as a disease with protean manifestations. The classical presentation of "stone, bone, abdominal groan and mental moan" is far too rare to be relied on. The signs and symptoms can be put into three groups, depending on their origin.

Skeletal Syndrome

Pain in bones and joints, spontaneous fractures, cysts in the bones of the skull, deformity of the long bones, kyphosis, scoliosis or other deformity of the thorax, waddling gait.

Urologic Syndrome

Nephrocalcinosis, renal calculi. There are varying figures reported for the frequency of primary hyperparathyroidism as the cause of renal calculi; the usually accepted one is from 5-10%.

Continued

Hypercalcemic Syndrome

With earlier diagnosis an increasing number in this category are being discovered, perhaps comprising 15% of cases. Symptoms include malaise, muscular weakness, bradycardia, psychiatric manifestations, polyuria, polydipsia and constipation. Polyuria and polydipsia are not infrequent complaints and may be due to the hypercalcemia itself rather than to renal insufficiency.

St. Goar[16] in a series of 45 proven cases had 16 in which gastrointestinal symptoms were a predominant feature and eventually lead to the diagnosis. Hypercalcemia causes a neuromuscular excitability, eventually leading to a decreased tone of the gastrointestinal tract. The large bowel atony leads to constipation while gastric atony results in dyspepsia, nausea and vomiting.

Frequently Associated Diseases

There are certain diseases which, because of their frequent association with hyperparathyroidism, warrant consideration of this diagnosis when encountered.

Peptic Ulcer

Hypercalcemia is capable of producing gastrointestinal symptoms, but in addition peptic ulcer can be demonstrated in 10-15% of patients with primary hyperparathyroidism. The increased incidence of peptic ulcer may be due to a direct action of parathormone on the gastric mucosa.[17] Children or young women with peptic ulcer should especially be investigated for hyperparathyroidism. The conventional treatment of peptic ulcer by milk in a patient with hypercalcemia may precipitate acute calcium intoxication.

Pancreatitis

Keating[18] recognized the significance of this association and also pointed out the difficulty in diagnosis.

Multiple Endocrine Adenomatosis

Hyperparathyroidism may be associated with hyperinsulinism and/or pituitary adenomas. It has also been reported in association with the Zollinger-Ellison Syndrome.

Problems of Acute Parathyroid Intoxication

Since Lowenburg[19] produced a hypercalcemic crisis in man by the accidental administration of an overdose of parathormone, it has been evident that hypercalcemic crisis can occur. Since that time, many cases have been well documented.[20] Wilson[21] recently reported a series and listed the clinical manifestations as follows:

CNS	GI	RENAL	CVS
Headache	Anorexia, nausea	Precipitation of calcium in renal tubules.	Supraventricular tachycardia
Restlessness	Vomiting		Shortened QT intervals (EKG)
Disorientation	GI hemorrhage		Circulatory arrest
Coma	Acute pancreatitis	Progressive oliguria	

There have been 27 cases documented, of which eight were operated upon and survived. In all but two, the serum calcium was greater than 17 mgm.%

However made, the diagnosis of primary hyperparathyroidism must be made with assurance, so that the surgeon may have complete confidence in making his dissection as radical as necessary to locate and remove the offending glands. The treatment of this disease is primarily surgical.

Case Report

A 25-year-old married white woman was admitted to Mount Sinai Hospital 6-8-64 for investigation of an elevated serum calcium first discovered a month earlier while she was hospitalized for an illness diagnosed as acute pyelitis. An intravenous pyelogram revealed minute sparse flecks of calcium in both kidneys. The serum calcium was elevated on two determinations. The patient had had two other episodes presumed to be kidney infections, both of which responded to treatment. There was no history of kidney stones, of excessive milk or antacid ingestion, or of vitamin D consumption. She denied weakness, emotional lability, cramps, epigastric pain, indigestion or hematuria. She thought she drank more fluids than normal, but denied having polyuria or nocturia. She had a chronic problem with constipation and if she did not take a laxative she would have a stool only once a week.

Physical examination revealed a well developed, well nourished white female who was very co-operative. The physical neurological examination was entirely normal except for mild tenderness at the left costovertebral angle.

Laboratory studies gave the following results: Hemoglobin 12.5 gm%, WBC 5,000 with a normal differential, hematocrit 39%, sedimentation rate 4 mm./hour, urinalysis negative. A number of serum calcium determinations (EDTA chelation method) gave levels of 10.6, 11.0, 10.8, 11.7, 11.8, 11.2, 11.4 mg%. Normal upper limit 10.5 mg%. Serum phosphorus measurements varied from 2.2 to 2.8 mg%. Serum sodium and potassium were normal. BUN was normal. The serum chloride was 109 mEq./L. Cholesterol was 125 mg%. Alkaline phosphatase was 10 KA units.

The patient was placed on a 150 mg. calcium intake for three days, following which 24-hour urinary calcium excretion was 222 mg., 239 mg. and 189 mg. The tubular reabsorption of phosphorus was 70% (normal 80-90%). Kinemometry was within normal limits. A rapid calcium infusion test was performed but gave confusing results which could not be interpreted.

Chest X ray was normal. A dental film showed the lamina dura to be present. Skull films, and upper GI series, and an electrocardiogram were all normal.

On 6-17-64, an operation was performed, and in the region of the right lower parathyroid gland an adenoma was discovered. The other parathyroid glands did not appear atrophic. The adenoma was an ovoid, moderately firm nodule weighing 1.35 grams, which on microscopic examination showed a mixed cell pattern composed of chief cells, transitional water-clear cells and a few aggregates of oxyphils. There was a thin, intact capsule and at one pole a small fragment of normal parathyroid tissue.

The patient's postoperative course was uneventful. Postoperatively the serum calcium varied from 8.5 to 9.3 mg%. The serum phosphorus level rose to 3.4 mg%, and the serum chloride was 107 mEq./L. The patient was discharged on 6-23-64 in excellent condition.

Allan Sniderman
Medical Clerk (Senior Medical Student)
Mt. Sinai Hospital

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6-21 Additional information can be obtained from the Grand Rounds Editor, Minnesota Medicine.

My sincere thanks to Miss Bernice Peckham, Librarian, Mt. Sinai Hospital Medical Library, for her assistance and encouragement in compiling this essay.

Fortune does not change men; it unmasks them. — Mme. Necker

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The initial response is usually maintained without dosage increases; indeed, initial dosage is often reduced for maintenance purposes.

Salicylate or steroid therapy can usually be diminished or, in some instances, eliminated.

Psoriatic arthritis responds in the same way as rheumatoid arthritis but the skin lesions are usually not affected either favorably or adversely by treatment.

Precautions
Before prescribing, the physician should obtain a complete history and perform a complete physical and laboratory examination, including a blood count.

The patient should be kept under close supervision and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools.

If coumarin-type anticoagulants are given simultaneously, the physician should watch for excessive increase in prothrombin time.

Side effects
The most common side effects are nausea, edema and drug rash. Infrequently, agranulocytosis, generalized allergic reaction, stomatitis, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug.

Contraindications
These include: edema, hypertension, or danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when other potent chemotherapeutic agents are given concurrently because of the increased possibility of toxic reactions; when the patient cannot be seen regularly; when the patient is senile.

Note: The physician should be fully aware of dosage, precautions, side effects and contraindications as contained in the complete prescribing information.

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Abstracts, Briefs and Commentaries

THE DURABILITY OF AORTO-ILIAC ENDARTERECTOMY, A ROENTGENOLOGIC AND PATHOLOGICAL STUDY OF LATE RECURRENCE

The authors present their results in the use of endarterectomy as a primary method of reconstruction in an occlusive process which is largely confined to the aorta and common iliac arteries, and they describe their technique and results in 104 cases of those operated. Certain classes of patients were excluded in order to investigate the persistence of good results and the incidence of recurrent disease in a minimum period of two years of observation. Sixty-seven total cases were submitted to the study; of these 67 patients studied there were 151 sites of operation.

In the follow-up angiographic studies there was an appearance of angiographic changes of either occlusion in 4%, or stenoses without occlusion in 41% of the 100 operated sites on the iliac artery. Of the 51 operated sites of the aorta, there was no evidence of occlusion, but there was evidence of partial stenosis in 15%. However, of all the abnormal changes noted, 84% were classified as class I, those in which narrowing was less than 30%. In the few recovered specimens it is interesting to note that the recurrent lesions showed true secondary atherosclerosis by gross and microscopic examination. The authors also point out that the endarterized segment does not re-endothelialize but, as confirmed by other studies, develops a pseudo-intima of organized fibrin deposits closely mimicking the pseudo-intima of the plastic arterial prostheses. The authors also felt that there was no significant difference between the use of endarterectomy in this type of patient and the use of arterial prostheses in the over-all long-term evaluation.

It was their conclusion that these observations in no way detract from the great clinical value of aorto-iliac endarterectomy but that they point up the obvious fact that the surgical treatment of arteriosclerosis is not lastingly curative. The authors also point out that in the nine cases followed angiographically for two years or more *after* the onset of recurrence, all showed progression in the arterial disease; of these nine patients, four had complete occlusion.

Continued

This is a very interesting paper because it indicates that significant atherosclerosis developed in the diseased arteries despite endarterectomy. However, they did not state whether arterial prostheses also developed atherosclerotic changes in the pseudo-intima, but did intimate that the end results were approximately the same. Other studies by DeBakey suggest, however, that the pseudo-intima of a prosthesis is less likely to develop atherosclerotic changes than the percentage recorded by these authors would indicate. Certainly this type of evaluation in long-term results needs continued careful survey. Furthermore, the authors did not reveal the exact status of the other adjunct medical treatments of atherosclerosis, i.e., the rigid control of diabetes mellitus, a low cholesterol diet, and abstinence from smoking and drugs. This type of observation would be extremely helpful in correlating concomitant medical control of and surgical procedure in atherosclerosis.

Jerome Grismer, M.D.
Minneapolis, Minnesota

Szilagyi, D. E., Smith, R. S., and Whitney, D. G.: The Durability of Aorto-Iliac Endarterectomy, A Roentgenologic and Pathological Study of Late Recurrence. Arch Surg 89:827, 1964.

GALLBLADDER DISEASE IN DIABETICS

Diabetics do not withstand the complications of gallbladder disease as well as other people.

Between 1947 and 1960 a total of 145 diabetics with cholelithiasis and cholecystitis were admitted to Massachusetts General Hospital. Mundth compares results in these cases with those in 150 nondiabetics operated on for acute cholecystitis.

Of the 145 diabetics 43 were treated without operation. Of the 102 patients treated surgically, 99 had a cholecystectomy with or without exploration of the common duct and three a cholecystostomy.

The operative mortality was 22 percent and the incidence of postoperative complications was 51 percent in the surgically treated diabetics, as compared with 0.7 percent and 11 percent respectively in the nondiabetics. Diabetics have a special liability to gallstones; incidence is 25 percent in diabetics against eight percent in nondiabetics.

Patients with mild diabetes tolerated elective biliary tract surgery very well. The operative mortality and morbidity were not significantly different from those in nondiabetics.

It is recommended that early elective cholecystectomy should be carried out in all diabetics known to have cholelithiasis, unless a specific contraindication is present.

Courtesy of World-Wide Abstracts

Mundth, E.: New Engl J Med 267:13:642

MAMMOGRAPHY

The Cancer Bulletin of December, 1962, came to my attention several months ago. It contained an extensive review of the research done by a group at the University of Texas M. D. Anderson Hospital and Tumor Institute on Mammography.

X-ray study of the female breast dates back fifty years, but it was not until recently considered of great practical value. This was attributed to poor X-ray equipment and tubes, poor and inexperienced technicians, and the inexperience of the radiologist. The Texas group, consisting of several specialists representing different fields of medicine, reported results of 2,000 mammograms on 1,204 patients in 1962. X-ray examination and diagnoses were made without knowledge of the patient's history or clinical findings. Working together with the Eastman Company, a much superior film was developed. The group also worked with research men from the manufacturers of X-ray equipment, with the result that technicians improved and radiologists matured in the interpretation of films.

The group invited radiologists to visit their organization to become familiar with their methods and avoid making the same errors they had made. Dr. Robert Egan, the radiologist playing a large part in the program at Texas University, is now at the Methodist Hospital of Indiana at Indianapolis, Indiana. Taking part in the mammogram study were 24 participating institutions, one of which was the University of Minnesota Medical School. All of their radiologists were given a five-day indoctrination in mammography. Two hundred radiologists have taken this course of training. Dr. Egan states that it takes two years to properly train a cytology technician and six months with accumulating experience for a pathologist.

I wrote to Dr. Egan personally for more information about their work and later publications, and received from him a fine personal reply, together with eight reprints concluding his work through 1964. He stated that interest had increased with the publications on the technique of good mammographs. Procedures had not been publicized to a great extent until fundamentals were established and it was recognized that good films were a necessity. The accuracy of interpretation of films improves with experience.

Dr. Egan had personally performed 3,818 consecutive roentgenographic examinations. He states that benign lesions interpreted as malignant were the greatest source of error. Eighty-five clinically unsuspected carcinomas were diagnosed. Co-operation with clinicians, surgeons, and radiologists is important, and nonpalpable lesions should be localized for the surgeon at the time of biopsy. Bilateral simultaneous carcinomas were detected by mammography in 3 per cent and bilateral successive cancers in 4 per cent of examinations. Cancer of the remaining breasts was found in 28 of 278 patients who had had one breast removed previously.

Collected data indicate that roentgenographic and pathologic diagnoses agreed in 85 per cent and that the correct diagnosis was 80 per cent for cancer by mammography and 90 per cent for benign lesions. X-ray study of the breast has now been extended to include the axilla.

Periodic radiographic examinations have been recommended. By comparison of films taken at six to 12-month intervals, slight changes occur that would not be detected without a series of films. By this means breast cancers have been diagnosed before there was any clinical evidence of their presence.

The very excellent article on mammography by Gersholn-Cohen in the December issue of Minnesota Medicine coincides with the results of studies here reviewed. His work is recognized several times by Egan. If anything, Dr. Egan and his colleagues report higher percentages of accuracy by clinical diagnosis (70 per cent), by radiologist (90 per cent), and by combined clinician and radiologist (95 per cent).

Continued

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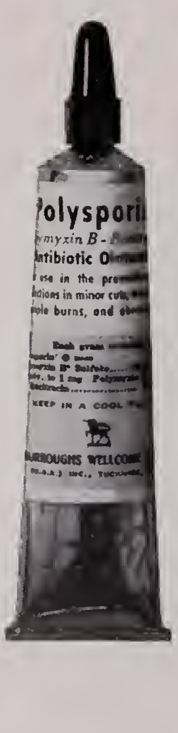

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Discussion

Dr. Egan graciously sent me eight reprints on technique and interpretation of films, with much data reported in the way of statistics. I am turning these all over to the Hennepin County Medical Society library.

They seem to feel that the surgeons have been responsible for part of the nonacceptance of mammography. My feeling is that not until recently has the procedure been presented in a convincing manner. Dr. Egan's group does not discount clinical study and examination but recommends a combined effort on the part of all concerned. They state that a diagnosis of carcinoma by mammography must be confirmed by biopsy before radical surgery, even to the exploration of all four quadrants of the breast in the case of a nonpalpable lesion.

They even had a pathologist review his gross specimen and found he had missed a very small carcinoma because he had cut his slices too thick.

We all know that carcinoma of the breast can be cured in a higher percentage of cases if the lesion is small and without metastases, regardless of how the early discovery is accomplished.

Stanley R. Maxeiner, M.D.
Minneapolis, Minnesota

COLON CANCER AND INGUINAL HERNIA

The authors report on 107 consecutive male patients with proven carcinoma of the colon and rectum who were treated at a Veterans Administration hospital between 1955 and 1961. During this six-year period 1,334 patients were admitted because of inguinal hernia. Thirty patients had both cancer and an inguinal hernia; of these, 18 first consulted a physician because of symptoms primarily related to the hernia. These symptoms included (1) pain over the hernia, (2) increase in size of a pre-existing hernia, or (3) recent recurrence of a previous herniorrhaphy. These symptoms should lead to suspicion of possible large bowel malignancy because they may indicate early lower intestinal tract obstruction. The authors believe that sigmoidoscopy and barium enema are mandatory in the preoperative study of all patients over 40 years who are being considered for elective herniorrhaphy.

Courtesy of References and Reviews
Journal of the American Medical Association

Terezis, N., Davis, W., and Jackson, F.: New Engl J Med 268:774, 1963

PERSISTENT CARCINOMA OF CERVIX

A pathological review of 83 pelvic exenteration specimens for persistent or extensive carcinoma of the cervix showed the carcinoma to be more extensive than clinically apparent. The urinary bladder was invaded in 61% of the cases and the rectosigmoid in 44%. A poor prognosis was associated with large bowel invasion, but 27.7% of the patients survived for five years. Survival was mostly dependent on finding lymph node metastases. The most characteristic alteration of irradiation was the finding of subintimal foam cell plaques in small arteries, especially near the sites of necrosis.

Courtesy of References and Reviews
Journal of the American Medical Association

Perez-Mesa, C., and Spjut, H.: Arch Path 75:462, 1963

GENTLE TREATMENT OF CLUBFOOT

Keim and Ritchie have reviewed a group of children with clubfoot in the Shriners Hospital in Winnipeg. The flattop talus is seen usually in the

Continued

treated case of clubfoot, and they demonstrate the "nutcracker" mechanism which tends to crush the talotibial articular surface, causing the flattop talus.

They refer to this mechanism as the "nutcracker effect" and in order to diminish this effect in manipulating an infant with a clubfoot they indicate that the simplest procedure is to loosen the hinge or pivot, the Achilles tendon. This can be done by early tenotomy, and it is a simple, effective procedure that can be done subcutaneously at one level in infants or at the three levels in older children. Maximum correction should not be attempted at one sitting. If the Achilles tendon or deltoid ligament prevents correction, it should be surgically released rather than risk crushing the talus, thereby causing a greater problem than would occur without treatment.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Keim, Hugo A., and Richie, Gordon W.: Nutcracker Pigment of Clubfoot. JAMA 189:613, 1964.

ADVANCED ISCHEMIA, RECONSTRUCTED PROCEDURES OF THE FEMORAL, POPLITEAL AND TIBIAL ARTERIES

These authors performed direct surgery of the femoral, popliteal, and tibial arteries in 206 patients with advanced ischemia of 216 extremities, 100 of these extremities facing immediate amputation. In 50% of the patients the surgical procedure extended distantly into the terminal popliteal, tibial, or peroneal arteries and consisted either of endarterectomy or bypass and thromboendarterectomy. Saphenous veins were used in the bypass procedure or venous patchgraft over areas of reconstruction. The over-all success rate was 82.9%, while the salvage rate in the extremities facing immediate amputation was 72.3%. The degree of improvement in the number of late failures was dependent upon the extent of the disease, particularly in the lower leg vessels. Although pulses were not always restored, even limited restoration of arterial flow was often adequate to halt gangrene, to heal ulcers, and to preserve a useful extremity. The results indicate that arteriography and surgical exploration of the vessels are indicated in all extremities in otherwise operable patients before resorting to amputations. An attempt to restore arterial flow should be made if one or more of the vessels or their equivalent are patent above the middle third of the lower leg. Surgery of the tibial arteries in most cases extended distally to the point of origin of the peroneal and the posterior tibial, and at times even further. Lumbar sympathectomies with removal of the sympathetic ganglion from L-2 through L-5 were performed as an adjunctive procedure in most patients.

This is a provocative article, indicating that even in the face of severe ischemia, diagnostic studies should be done. This is especially true in individuals about to undergo amputation. The authors did not classify the other types of concomitant diseases that might be present, such as diabetes mellitus. However, individuals with such diseases were undoubtedly presumed to be included in this series. The success rate was astonishingly good, even though in 20 patients there were late occlusions three months to five years after the procedure. But even though some had late

Continued

occlusions, approximately 30% suffered only minimal symptoms; therefore surgical procedure was of value. Of the 206 patients, six died immediately after surgery. In four cases the cause of death was not related to the surgery; in two death resulted from myocardial infarction. This points up the fact that these individuals had disease other than in the vessels.

Jerome Grismer, M.D.
Minneapolis, Minnesota

Harrison, J. H., and Preez, A. R.: Advanced Ischemia, Reconstructed Procedures of the Femoral, Popliteal and Tibial Arteries. Arch Surg 89:817, 1964.

VERTICAL VERSUS HORIZONTAL INCISIONS

From the department of surgery at the University of California in Los Angeles, Halász compares a number of complications and sequelae associated with these types of incisions, using 50 patients in each series.

This was not a double blind study, but the two series were reasonably identical.

It appears that the major complications were those for pulmonary diseases. In the patients with vertical incisions there were ten pulmonary complications as against one in patients with transverse incisions.

It would appear from this study that the transverse incision offers some advantage in diminishing the incidence of pulmonary complications. This is explained on the basis that in the vertical incison a greater number of peripheral nerves are involved than are encountered in a transverse incision; this in turn restricts the adequate ventilation of the lungs and increases pulmonary complication. We should have no fear of deviating from the time-honored ritual of making muscle-splitting incisions, and should have no hesitancy in cutting transversely the rectus sheath and muscle.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Halasz, Nicholas A.: Vertical vs. Horizontal Laporatomies. Arch Surg 88:901, 1964.

The Small Intestine

"Anatomists have divided the small intestine into three divisions. The first eleven inches of its length is the *duodenum.* This comes from the Latin 'duodeni' (twelve) because the early anatomists measured by using their hands as convenient rules and the duodenum is twelve finger-widths in length. The Germans, who are much less patient with classical derivations than we are, called the duodenum *zwolffingerdarm,* which is straight German for 'twelve-finger-intestine.'*

The next eight feet of intestine is the *jejunum,* from the Latin 'jejunus' (empty), because the Roman medical writer Celsus thought it retained no food but merely sent it on. The remainder of the small intestine is the *ileum,* a Latin word that comes perhaps from the Greek 'eilein' (to roll up) because that is what must be done to the small intestine if it is to be made to fit in the abdomen."*

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*Asimov, Isaac: Words of Science, Houghton Mifflin Company Boston, 1959, p. 79.

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Book Reviews

Until you put a thought in words — sharply and precisely — it isn't a thought at all; it is just a kind of fog rolling around inside the skull. — John Fischer

CARDIAC ARREST AND RESUSCITATION — **By Hugh E. Stephenson, C. V. Mosby Company, St. Louis. Second Edition 1964; 501 pages, $15.00.**

Dr. Hugh Stephenson is Professor of Surgery at the University of Missouri. He has collected in his department a file of over 1700 cases of cardiac arrest reported by some 700 physicians and this book represents the fruits of his studies of this unique collection. Although the first edition is only six years old the advances in this field have been so rapid that the new edition is justified. Every physician who may face the problem of cardiac arrest (and this means every physician) can profit from this book. Cardiac arrest, in the first minute or two, may be a completely reversible complication. To cope with this catastrophe demands a plan of action worked out in advance. There is no time for consultation with the cardio-pulmonary experts; the fate of the victim is decided primarily by the action of the attending physician on the scene. It is with this "first aid" that Stephenson's book is chiefly concerned.

The opening chapter deals with the historical background of cardiac arrest and resuscitation. Ventricular fibrillation has been known since Vesalius' time. Electric current has been used to revive the arrested heart for over one hundred years ago.

In the chapter on the mechanism of cardiac arrest are case reports indicating the universality of the problem throughout medicine. The diagnosis of cardiac arrest is usually made without difficulty: no pulse, respiration, or gasping is present. The patient appears dead. Stephenson warns against diagnostic frills, (including auscultation!) being too time-consuming.

"The delay in making a diagnosis of cardiac arrest is responsible for the bulk of the failures of resuscitation. Until the simplicity of making a diagnosis of cardiac arrest is understood, it is likely that the appalling mortality from episodes of sudden failure of the heart will continue. We still believe that the best rule of thumb is that if there is no palpable pulse and no obtainable blood pressure, both of which have disappeared suddenly, then the diagnosis of cardiac arrest can be made with every reasonable degree of assurance. Let those who disagree assume the burden of proof that under such situations the cardiac activity is sufficient for life. Again let us emphasize, more patients lose their chance for recovery during this crucial period between arrest and diagnosis than from any other aspect of the resuscitative procedure. The time factor represents the crux of successful resuscitation. Few patients can survive after a delay of more than four minutes before artificial circulatory activity is maintained by manual systole. Since the period of reversibility is almost always present in cardiac arrest, it is tragic to allow this period to pass in following time-consuming diagnostic procedures such as searching frantically for a stethoscope or trying to obtain consultation from others. The patient's chance for survival rests with the personnel who are with the patient at the time of arrest."

Reuben Berman, M.D.
Minneapolis, Minnesota

FITNESS FOR THE WHOLE FAMILY — **Paul Dudley White, M.D., Curtis Mitchell, Doubleday and Co., Garden City, N. Y. 1964, 302 pages. $4.95**

This book has been edited by two men who have had a sincere interest in the health of many of our well-known national figures. It is a compilation of the observations and opinions of 15 or 20 health and exercise consultants or writers who have been interested in physical fitness from a sincere desire to promulgate better health without confusing it with the commercial aspects, as is sometimes done by the faddists.

As Mitchell has so aptly pointed out, "Mankind is currently immobilized by comforts, conveniences, and chemical cures." Dr. Paul Dudley White has stated that the time to prepare for fitness after you have retired is to do it when you are still young. He indicates that physical fitness should become a habit acquired in youth. He points out that it is better to wear out than to rust out, and that the rusting process is much faster when you are inactive.

This book can be recommended to all doctors, and all doctors should be able to recommend it to those patients who wish to introduce physical fitness into their mode of living.

Carl O. Rice, M.D.
Minneapolis, Minnesota

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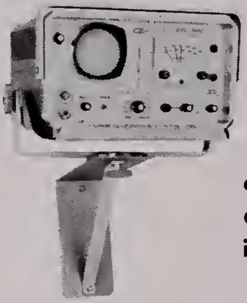

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Perinatal Mortality Study

Diabetes Mellitus and Pregnancy*

Case Report

This was the fifth pregnancy of this diabetic, 44-year-old, Rh positive mother. During the pregnancy she was maintained on 50 to 65 units of Lente insulin daily. During the first trimester she had a large buttocks abscess treated with penicillin and tetracycline. On prenatal examinations her urinalyses were always negative for sugar.

The mother was admitted to the hospital at 36 weeks of gestation for observation and management. She was not in labor. On admission, her fasting blood sugar was 104 mgm.%, hemoglobin 11.1 gm.%, white blood count 6,600 per mm.^{3}, and urinalysis negative for sugar and albumin. An admission electrocardiogram showed incomplete bundle-branch block; her blood pressure remained within normal limits. Her Lente insulin dosage was decreased 5 units daily, from 50 units on admission, to 25 units, at which time her urine showed 3 plus and 4 plus glycosuria; the dosage was then increased to 35 units daily. A fasting blood sugar done two weeks after admission was 270 mgm.% (no fasting blood sugars had been done during the two weeks after admission). Also, the fetal heart tones, which had been listened to and recorded daily, were absent two weeks after admission. After four days of absent fetal heart tones, an abdominal X ray of the mother showed air in the biliary tree and umbilical vein of the fetus, with a question of air being present in the fetal heart. Immediately following the abdominal X rays, the mother received two ounces of castor oil orally, which induced labor, and the next morning she delivered an 8-pound, 3-ounce, 21-inch, macerated male stillborn infant at 38½ weeks of gestation. No autopsy was performed on the infant. Two days following delivery, the mother's fasting blood sugar was 375 mgm.%; the Lente insulin was then increased from 35 to 40 units daily.

The mother was discharged one week following delivery with no repeat determination of the fasting blood sugar. Her daily urinalysis on 40 units of Lente insulin varied from 1 plus to 2 plus glycosuria.

Comment

The Ramsey County Perinatal Mortality Study Committee evaluated the care that the mother received during her pregnancy.

1. With diabetes mellitus of such severity, the mother should have been delivered at 36 to 37 weeks of pregnancy, instead of waiting until closer to full term. Concerning pregnant diabetic patients, Reid[1] states: "To avoid fetal and maternal accidents, premature termination, at least by the 36th or 37th week of pregnancy, has been advocated, and there are some authorities who believe that this should be a routine practice. The added maternal risk incurred by this policy is real, however, for it often necessitates delivery by cesarian section. At the same time, as stated before, a large proportion, possibly one third or more, of the fetal deaths in diabetic pregnancies occur during the last few weeks without warning or demonstratable cause. What is more disturbing is the fact that in these patients there is no detectable clinical toxemia, and their diabetes is metabolically well controlled." Thus, in the present case, even though the diabetes was not ideally controlled, the fetus still may have died before full term even under ideal insulin control.

2. The medical care of the mother's diabetes in this case was not adequately controlled. With a normal fasting blood sugar obtained on 50 to 65 units of Lente insulin daily, her dosage should have remained at that level, rather than lowering the dosage to 25 units of Lente insulin daily with resulting 3 plus and 4 plus glycosuria and even a fasting blood sugar of 270 mgm.% when the dosage of insulin was raised to 35 units daily.

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*Ramsey County Perinatal Mortality Study Committee.

Continued

Furthermore, the mother should not have been discharged home with 40 units of Lente insulin daily when she had a fasting blood sugar of 375 mgm.% along with 1 plus to 2 plus glycosuria on 35 units of Lente insulin daily.

With proper medical care of severe diabetes mellitus in pregnancy, along with induction of labor at 36 to 37 weeks of pregnancy, it is hoped that more infants born to severely diabetic mothers can be salvaged.

Reference

1. Reid, Duncan E.: A Textbook of Obstetrics. W. B. Saunders Company, Philadelphia, Penn., page 840, 1962.

Ten Commandments to Prevent Alcoholism*

PHYSICIANS should instruct their patients to follow these ten rules to avoid the development of alcoholic dependency:

1. Never take a drink when you "need" one.
2. Sip slowly and space your drinks: the second drink 30 minutes after the first; the third an hour after the second; and never a fourth.
3. Dilute alcohol. Have a long, weak drink — never on the rocks, never straight and never, never out of the bottle!
4. Keep an accurate and truthful record of the amount and number of drinks you take.
5. Never conceal the amount of alcohol you drink. Instead, exaggerate it.
6. Do not drink on an empty stomach.
7. Stop drinking on signal. The signals are: "luncheon," "left office," "on the way home," "before dinner," "before bed," "meeting people," "celebrating" and "to get me through." Substitute something in place of alcohol at these times, such as a big cup of hot, strong tea before dinner to refresh and energize (mountain climbers drink tea, not alcohol).
8. When tired or tense, soak in a hot tub and follow with a cold shower.
9. Never take a drink to escape discomfort, either mental or physical.
10. Never, never take a drink in the morning, thinking it will offset a hangover.

Avoid alcohol dependency as you would the plague. It is most insidious and unless you are very careful, it will steal up without your knowing it.

William B. Terhune, M.D.
New Canaan, Connecticut

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*Reprinted from The Ten Commandments to Prevent Alcoholism, New York J Med, August 15, 1964.

Derivatively Speaking

Carbuncle derives from the Latin *carbunculus* (a little coal), diminutive form of *carbo* (coal). Red stones (the ruby and the garnet) were called carbuncles because they resembled glowing coals. Later the term carbuncle was used to designate a red spot of inflammation on the surface of the skin, originating in the tissues and looking and feeling like a glowing coal.

The past always looks better than it was; it's only pleasant because it isn't here.
— Finley Dunne

History of Medicine

Harvey Cushing — Part II*

(1869-1939)

Since the life of Harvey Cushing was portrayed in this department last month, we have received permission to add some personal reminiscences by one of Doctor Cushing's former pupils at Johns Hopkins. Carl W. Rand, M.D., of Los Angeles, furnishes some interesting anecdotes about his great teacher.

"I do not remember exactly when I first heard of Doctor Cushing, probably very early in my student days at the Hopkins; but certain it is, that stories of this gifted, energetic, young brain surgeon were impressed upon me before I had entered upon my clinical years . . . My formal introduction, however, came most unexpectedly in my junior year. Doctor Cushing gave an elective course in dog surgery, which proved to be the most popular in the school, and lucky indeed were the students who were enrolled. It was held in a small brick building — the Hunterian Laboratory — which was about as crude and crowded as that in which the "great John" had once worked. But with Doctor Cushing passing from group to group the class was on the *qui vive,* and many a trembling incision and faltering stitch were made under his penetrating eyes. He was a master surgeon, and would tolerate no mediocre performances. On the day in question it had fallen my lot to take the part of anesthetist, the "patient" being an unusually large and somewhat vicious dog, whose teeth were prognathic, and who did not take kindly to the idea of being put to sleep. And when one considers that he was strapped on his back on a hard table with his legs pinioned down, one could hardly blame him. The cone, in which rested the sea sponge upon which the ether was poured, barely covered his dark muzzle, and I was having a desperate struggle to get him under. During a lull in the fracas, I suddenly became aware that Doctor Cushing was standing directly behind me. I tried frantically to suffocate the "patient" before being reprimanded, but to no avail. Finally with a very red face and forced grin, I turned apologetically and said in a hesitant voice: "He's a pretty big dog and I can hardly get the cone over his nose." To which Doctor Cushing replied with a toss of his head and a pat on my shoulder, — "Don't blame your golf balls," — and walked on. Whether or not he appreciated the humor of the situation, I never knew; I believe he did.

My next intimate experience with him occurred two years later, when I was an intern. By then we had learned that "Cushing patients," especially those harboring brain tumors, were to be most closely watched. Their every sign and symptom must be recorded in minutest detail. It happened that a man with high intracranial pressure, secondary to a suspected tumor, came under my care. One afternoon, on going into the ward, I noticed that he was cyanotic and gasping for breath. As I stood by the bed he stopped breathing, although his heart continued to beat. Instinctively I climbed upon the bed and started artificial respiration, impulsively telling a nurse to send for Doctor Cushing. Upon arriving, he took in the

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*See Minnesota Med 48:283, 1965.

situation at a glance, told me to "carry on" and ordered the surgery to be set up at once. With the patient finally in the prone cerebellar position on the table, he deftly shaved a patch of hair, made a quick incision and trephined the skull. He then carefully introduced a ventricle needle directly into a cerebellar cyst, and yellow fluid escaped in a parabolic stream. It somehow reminded me of blood letting. How he knew the exact location of the lesion, for he had had scant time to examine the patient, is still a mystery to me. In a few minutes spontaneous respiration was again established and my tired arms were given rest. A few days later I watched Doctor Cushing with his deliberate and meticulous technique, remove a large cystic astrocytoma from this same patient. The man recovered and was given many years of useful life.

During the World War I had tried repeatedly to secure detachment from the backward area in which I was stationed, in order to see active work at the front. All efforts through military channels failing, I wrote a personal letter to Doctor Cushing, who was then Chief Neurosurgical Consultant in the American Expeditionary Forces, asking transfer for duty under him. Within a week, in some mysterious way, I received orders to report at a certain camp, where a neurosurgical operating team was awaiting me. Doctor Cushing had arranged it by some direct method known only to himself.

His methods of treating head wounds at the front had proved revolutionary and many lives were thereby saved. I think he took deep satisfaction in visiting his various 'teams' who were carrying out his operative technique. On one round of inspection he happened into a tent hospital and found me in the act of removing a piece of shrapnel from a soldier's brain. I became aware of him standing behind me and felt a good deal as I had when he watched me trying to anesthetize the dog years before. I even wondered about my 'golf balls'; but peering over my shoulder he said quietly 'good work,' thus dispelling my apprehensions."*

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* Rand, Carl W. Doctor Cushing as I knew him. Los Angeles Neurological Society, Bulletin. 5:1,2,3,6,7, March 1940. By permission.

History of Medicine in Wright County*

Dr. Suttan, according to an item from the Howard Lake correspondent in the *Delano Eagle* of October 16, 1884, was building a large addition to the Dr. Ball Building. Nothing else is known of him, not even whether he really was a physician.

Wilfred (P.) Tessier, a graduate of the College of Physicians and Surgeons, Minneapolis, in 1887 may have practiced in Wright County for a short time in that year. A news item (*Delano Eagle,* July 28, 1887) tells that "Dr. Tessier of Minneapolis is locating here. We understand he formed a partnership with Dr. Mignault" and in October (*Delano Eagle,* October 20, 1887) we learn that "Dr. W. P. Tessier has started for Annandale where he intends to locate."

This is all the information about him that could be found.

John J. Catlin, M.D.
Buffalo, Minnesota
Robert Rosenthal, M.D.
St. Paul, Minnesota

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*See Minnesota Med 48:537, 1965.

A married woman's as old as her husband makes her feel. — Arthur Pinero

Special Report—

*The General Practitioner and the Price of His Recovery**

H. P. VAN CLEVE, M.D.
Austin, Minnesota

THE GENERAL practitioner is disappearing from the American scene. Perhaps we should merely celebrate his demise as a needless vestige of an outmoded culture.

I want to present to you two case histories which perhaps will illustrate for you the strengths, the weaknesses, and the problems confronting the general practitioner today.

Case Report

The first case is that of a forty-one year old housewife who came to see me complaining of chest pain. In the way she presented her story it was obvious that she was concerned about her heart. At forty-one she certainly was not a likely victim of coronary artery disease and the description of her pain also did not point in this direction. However, she was overweight and somewhat hypertensive. Physical examination revealed no other abnormalities.

I had known this patient well for several years. She had four children, aged 5, 11, 13, and 15. Her husband was a repairman, and the family economically was caught in that common squeeze where their income did not quite meet what they felt to be their needs. At various times I had seen all members of the family and had made calls to their home. She was much like a mother hen, deeply concerned over her brood, but not much of a housekeeper. I had cared for one of her children just after the family had moved to town. The child had had extensive medical care in a large city where many examinations had failed to demonstrate specific disease but borderline findings indicated something might be present. A letter from the pediatrician had read, "We have never arrived at a definite diagnosis but felt that possibly a mild glomerulonephritis was the best explanation for her elevated sedimentation rate and urinary findings." Maternal anxiety and medical uncertainty had resulted in six months loss of schooling for the child, most of which was spent in bed. At that time, after much discussion, the mother had accepted my recommendation that it was time to fish or cut bait and we should try getting the child up. We did and all went well. (Eleven years later the child is still well; the original illness is still unexplained). So I know this patient and her family quite well.

I sensed her pains were functional, but what had caused them? I said, "I've known you and your family for some time and yet I know very little

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*This paper was presented on May 8, 1964, at a seminar at the Ambassador Motel, Minneapolis, on undergraduate medical education held under a grant from the Hill Family Foundation by the Clinic Directors Committee of the Medical School. At this time Doctor Van Cleve was serving for a one-month period as an assistant professor in the Comprehensive Clinic Program of the Medical School under a grant from the Hill Family Foundation. His responsibilities centered about teaching personal medical care to the senior medical students in the outpatient clinic.

Continued

about you personally. Tell me something about yourself." With no more encouragement she told of a father that had deserted her mother when she was an infant. Her mother had remarried and she had had a happy childhood and looked on her stepfather with the love of any child for her own father. Several months before coming to see me, her true father had written her and told her he had remarried and that his second wife was dying of cancer. Would she please come and help him take care of her? It was a real sacrifice for her to go, but she went. Shortly after she arrived, her father showed his true colors again and again walked out, leaving her to care for a woman whom she had never known while the woman gradually succumbed to cancer. On completing her story, she paused a moment and said, "I don't know why I am burdening you with my troubles." I told her, "I asked you to." After still another pause, she looked up and asked, "What has this got to do with the pain in my chest?" I replied, "I think it has a lot to do with the pain in your chest." She got up, tidied up her appearance for her departure, hesitated at the door, looked at me and said simply, but with much feeling, "thank you," and departed. In the nine years since this episode, I have seen her many times, sometimes for herself, sometimes for her children. She has had occasional episodes of anxiety, mundane problems such as sore throat, and so on, but never has she had a recurrence of her chest pain.

I give you this case history because it illustrates some very cogent advantages of continuing medical care, the kind of care most readily given by a family physician. Let's look at the way this same patient would have been treated at a major medical center. A more detailed history — medical history, that is — would have been obtained. A complete physical would have been done. It is most likely she would not have escaped without some basic laboratory tests, a chest X-ray, and an electrocardiogram. Her painful, personal story would probably not have been elicited. I am sure the same diagnosis would have been reached by the physician and probably would have been conveyed to her in some such manner as "There is no evidence of trouble with your heart. Your pains are related to your emotional problems." The patient is left with many doubts such as "If the doctor is so sure, why did he do all those tests? Maybe he just couldn't find out what is wrong." If the patient had been referred to a psychiatrist, she probably would have ended up with a true understanding of her emotional problem, but meanwhile she would have spent a good deal of money the family could ill afford. She also would now have the feeling of guilt concerning this expenditure and, I believe, some increased insecurity to think that she could have been so "shook," so to speak, that all this had to be done to get her straightened out.

I am not very proud of the second case. In fact, it is quite painful to me to give it to you. However, as the first case illustrates the family physician functioning well, this case shows the reverse and illustrates the shortcomings of the family physician, shortcomings partly of his own making, and partly due to responsibilities forced upon him which he rather would not bear.

Case Report

A nine month old infant, was admitted as an emergency because of moderately severe dehydration. I was on emergency call and was not the usual physician for the family. History revealed the infant had had vomiting and diarrhea of several days duration. During this time his diet had consisted mostly of boiled skim milk. He was irritable and his temperature was 102° rectally. Examination revealed no other significant pathology. Having drifted away from doing much pediatrics, it has long been my policy to get pediatric consultation on all pediatric admissions. Our pediatrician had left the community and pediatrics shortly before as he could not stand all the calls and the continuing pressures of being a family doctor to children. It was a weekend and no other consultation was easily available. The problems of rehydrating the infant did not seem too complex. A standard text was consulted and fluids started accordingly. The child's temperature dropped overnight and he looked much better but was quite lethargic. Urine output was good. Fluids were continued at a rate suggested by the text. About twenty hours after admission the child suddenly convulsed and stopped breathing. Prompt efforts at resuscitation failed. An autopsy revealed cerebral edema. A recapitulation of the case showed that in spite of administration of fluids by a standard recent text, fluids actually were almost double what were recommended by other authorities and this undoubtedly had resulted in the cerebral edema and death.

I believe this sad case illustrates some of the basic problems confronting the family physician today. All of us in a major emergency may be forced to render care we were supposedly trained to handle but which we no longer can give with great facility. For example, if the Twin Cities were hit by an atomic bomb, most if not all of you who survived would find yourselves doing general practice, that is, taking care of all who came, regardless of their problems, in the best manner in which you were able. I am sure even the thought of learning to function in such a role is quite disquieting. While it is unlikely this will ever happen to you, to some degree it happens to the general practitioner frequently. When all is going smoothly, he handles those problems which are well within his scope of practice and refers those he is unsure about to someone else. All too often he is confronted with having to function in areas in which he feels limited because, firstly, no readily available consultant can be called in, and secondly, the problem doesn't appear to be serious enough to justify moving the patient a long distance to another medical center.

These two cases describe the general practitioner both when he is at his best and at his worst. Obviously his education must change so that he can function most of the time at his best and never, if that is possible, as illustrated in the second case. How? Well, here is what I believe! If the general practitioner is to survive, and survive he should, he must be educated better, he must be educated differently, and he must continue to be educated until the day he quits. He will not survive so long as his colleagues feel that he is a second class physician. His role and his preparation must be such that he no longer needs to look at the specialist and say to himself, "Anything I can do you can do better." He must be so trained that he can look the specialist in the eye and say, "Go ahead and treat disease, I'll treat people."

Training the General Practitioner

Dr. Dicks, an Englishman, writes the following about the present training of the general practitioner:

"I hold that the discouragement of the G.P. begins from the day he enters the hospital as a clinical student. The social and scientific prestige structure of the teaching hospital is created by the demigods of specialisms, who, even if modestly endowed, can still lord it within the kingdoms of their own firm and wards. . . . The student will tend to identify himself with these teachers, hoping he will be like them, have their skill, and emulate their practice and their manner, perhaps also their pomp and worldly success. The 'ideals' set before future G.P.'s are thus not older, wiser G.P.'s, but a series of figures of supposedly superior ability who have each mastered some special skills, to none of which our student can hope to attain.

"In fact these mighty consultants do not teach the G.P. more than a fraction of what he finds it useful to know. Yet, owing to identification and prestige, he still feels he has learned 'his medicine' and 'his surgery' from them and ought to be very grateful. Actually, what he has seen impressively in action has been the full-scale clinicopathological method applied to 'good teaching material — i.e., to patients with well-marked structural or biochemical change, where by a series of well-judged tests, recorded on charts of many hues, the right diagnosis fell into the team's lap. The image of good doctoring was that of the 'great white chief' performing miracles of mechanistic skill on a dramatic, perhaps catastrophic, but rare case, while the dull sort of case, whose pain did not fit in, was perhaps half-jokingly referred to 'our psychiatric colleague.' Interest in the common disease and worries of human beings was seldom shown, while the psychiatrist's field was too remote and creepy for sound practical men."[4]

Dicks says further: "I hold that the good general practitioner is the pivot of all adequate personal, friendly care for sick people and of preventive watch over the health of families and work groups. He could be, and often is, adviser and counsellor in matters often far removed from what is taught in hospitals but close to human health and happiness. To fulfil this role he ought therefore to have the opportunity to cultivate from the beginning of his medical studies the widest vision of human beings and their manifold troubles. This implies that from the first he must be introduced to the concepts of personality and culture-pattern, and not only to theories about chemicobiological mechanism or, at best, organism.

"To sustain his orchestrating function in relation to his client's condition, he needs to know enough about special techniques of diagnosis and therapy to decide when to call

Continued

in a technician (surgeon, psychiatrist) and how to evaluate the latter's advice. He need not be a master of any of these special crafts. His is the synthesising, presiding role — a role which the general hospital physician is apt to arrogate to himself, with far less claim to adequate knowledge of the patient."[4]

This indeed involves some basic changes in our current concepts of physician education. Dr. Dicks then proceeds to make many excellent recommendations for changes both in premedical as well as in medical education. To list his recommendations would make this paper too long but I do want to give you his introductory remarks:

"In attempting the following outline of education in a broad human medicine, I make the following assumptions:

"That we really desire, in the general medical course to produce a general practitioner, rather than offer a course of bits and pieces, vaguely making propaganda for the superiority of hospital practice.

"That this training should prepare *all* doctors, but especially general practitioners, to be competent to handle the psychosocial relations as well as the physical factors in the promotion of health and efficiency in individuals and groups, and in the reduction of human suffering.

"That specialization is and will remain a postgraduate task.

"That, training matters apart, the conditions and status of general practice will be so altered as to remove the present negative incentives which operate against the entry of highly gifted doctors into it by promoting the reforms advocated by Collings — e.g., grouped practices, finance, access to hospitals, and integrating responsibility for patients."[4]

No amount of polishing the present vehicle of medical education and practice will draw students into general practice. We need a new car. What is the alternative? Where will the present vehicle take us? Let me give you a few figures, a few quotations, and a Jacob Marley peck into "Christmas yet to come."

As you know, the general practitioner is truly disappearing from the American scene. In 1931 general practitioners constituted 71 per cent of all physicians in this country. In 1962 this percentage dropped to 27 per cent.[1] Only 20 per cent of medical school graduates today indicate they will go into general practice. An unknown percentage of these — but a sizeable one — will leave general practice after varying periods of time for specialty training. If these trends continue, the general practitioner will not be a significant factor in the practice of medicine 25 years from now.

T. F. Fox, an Englishman, made a survey of American medicine, its present and future, and wrote a lengthy treatise appearing in the "Lancet" for April 2, 1960. He made many interesting observations and some very pointed comments. Among them he says:

Replacing the General Practitioner

"Perhaps I am wrong, but I should guess that in the prevailing culture of the United States, the independent personal doctor is going to be specialized out of existence, and that within a few decades medical care will mostly be based on the hospitals."[5]

If the personal physician is to disappear, I would suggest that he will be replaced in any one or a combination of three ways:

1. He may be replaced by a hospital type practice as suggested by Fox. This is largely extant in England today.
2. He may be replaced by an internist-pediatrician team.
3. He may be replaced by technicians as is the case in Russia today.

The first two of these are already taking place in part. All three have glaring faults. George James, Commissioner of Health for New York City, writes "The executive with a polished walnut desk can usually arrange to leave his office for an hour to see a private physician. The unskilled worker in the shipping room, newly arrived from Puerto Rico, cannot so easily take the hour, and he has no private physician anyway, so what he may need is several four hour periods of waiting in each of a long series of specialized clinics." Thus, he does not use such care even if it is free. Instead, he will tend to utilize hospital emergency rooms and get "episodic, inadequate care."[7]

Hospital Practice

This states the resistance of the affluent to hospital practice and the inability of the marginally employed to avail themselves of such services. In addition, hospital practice for the 45 per cent of our people living outside the big urban areas is a complete impossibility. But this may come, nonetheless.

Internist-Pediatrician Team

The internists and pediatricians have already clearly indicated their lack of interest in filling the role of the general practitioner. Only 25 per cent of the decrease in the general practitioners has been replaced by internists and pediatricians. In addition, these have gravitated to the urban areas whereas the distribution of the general practitioner has remained distributed as before. As mentioned, in my city of 25,000 people, we lost our pediatrician. He left the practice of pediatrics completely for a job that freed him from the pressures of being a general practitioner for children, even though this involved a 50 per cent cut in his income.

Technicians

I have been given to understand by one of the staff just back from the west coast that there was much talk about the third alternative, namely the training of technicians. I have found no one who has dared to suggest this in writing. I have found many who have decried the possibility. Fox says: "When personal medical care is abolished, it is sooner or later reinvented. Thus, even under the Soviet system, the Russian leaders have personal physicians. It is the natural and sensible thing to do, and they can afford to do it. So should we."[5]

The Russian masses, you will recall, depend on technicians.

The Too Busy General Practitioner

There is one other fault of the general practitioner which I should discuss. He is much too busy. He has been unable to change the ecology of his society.

The average patient sees a physician three times as often today as he did 30 years ago. Remember also that there are only about one-third the number of general practitioners as thirty years ago and our population has doubled. This means that the average general practitioner today must see 25 or more patients per day plus innumerable telephone calls. He finds that either he cannot give the time he wishes to his patients or he must refuse care when called upon. He finds himself in a hopeless bind.

His public image has been severely damaged by refusing care in some cases or by insisting upon seeing the patient in the office because of lack of time. Any good practitioner today finds himself in this dilemma.

If he cuts his practice by refusing care, he is criticized. If he raises prices to cut his practice, he is criticized (plus the fact it doesn't work). Most drift into a sad third alternative, namely that of spreading himself so thin that he ceases to give satisfactory personal care. At this point his practice automatically starts to limit itself. This fault, that of being too busy, can only be remedied by graduating more general practitioners. Otherwise, it will get worse, not better. Freed from the tremendous volume of patients to see, the general practitioner could then function in the way he should function, "looking after people as people and not as problems."

Conclusion

In conclusion I would like to quote at some length, Iago Galdston. At the conclusion of his article entitled "The Birth and Death of Specialties," he comes to a conclusion different from that of Fox. He states:

"What I mean to convey is this: the future of medical service is not to be envisaged as a continued refinement, as well as increase, in the specialties, with the consequent parceling out of the patient to a host of men, who will care for him and treat his illnesses. I think rather that within two generations, that is before the second millennial year is reached, medicine as a science, and medical service perforce, will have undergone a revolutionary change, in many respects as profound as that effected by the rise of bacteriological

Continued

sciences. This revolution will not be brought about by the economic, legislative, or social manipulations of well-meaning men but by the maturation of those knowledges and intelligences embraced in physiological, and in ecologic, medicine. Unless global disaster puts an end to civilization and to science, the eventuations I have sketched are to my mind inevitable.

"I am conscious of the fact that in my presentation I have been somewhat light in my treatment of present-day medicine, including its specialists. I may have thus given you an erroneous idea of the esteem in which I hold contemporary medical science with its practitioners. I deem them both of the highest order. Were I grievously sick and had I the choice to be sick in any age in history, from the time of Hippocrates to the present, I would choose none but the present. For at no time in the history of man has the practitioner of the healing art been as tutored in the skills and as well armed with as great a multitude of means to fend against the ravages of sickness, and even more against pain and suffering as he is today.

"But as I have argued and as is clear to all thinking men, the treatment of disease is not the equivalent of the promotion of health, and well-being — and specialists treat disease.

"I am not so sanguine in my hopes for mankind, nor so naive, as to believe that man will ever so manage his life as to have no need for 'cures' and for the specialist who ministers them. I can envisage an attrition in specialties and specialists but not their total elimination from the medical scene or corps. It is only that I can see the future of medicine as lying in directions other than greater and ever greater specialism.."[6]

The doctor in active general practice today is making great strides at keeping abreast of new medical developments. He does need continuing medical education. The program in which I have been involved, namely teaching personal medical care to the senior medical students, has, I hope, been helpful to the students for it has certainly helped me to broaden my horizons and to develop an increased awareness of the rapid growth of medical knowledge. I believe an expansion of this program plus other new techniques would be tremendously helpful in keeping the general practitioner not only well informed but also an active, participating member of the medical family. But all such efforts will not be enough if those of you in medical education do not succeed both in modifying the educational climate from which the general practitioner must come, and in modifying his training program so that he may function with skill and pride as a knowledgeable family physician. If this cannot be done, new students will not be attracted to general practice and the general practitioner will ultimately disappear. The American public will be the loser.

Addendum

This paper has dealt with the problems of education of the general practitioner. It has not dealt with the many socio-political aspects which also affect his future, such as the general practitioner's role under socialized medicine, should such a situation evolve. Anxiety over his status as a general practitioner in a socialized medicine milieu was the reason most frequently mentioned by students for avoiding general practice.

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11-17 May be obtained from the author or the reprints.

Medical Economics

Health and Accident Insurance

"How much health and accident insurance should I carry?"

In undertaking to answer that question, it is important for the Doctor to remember that health and accident insurance is disaster income, and that it is neither necessary nor prudent to carry insurance equal to his earned income. It is essential merely that he have enough income to assure the basic necessities for himself and his family and to meet any fixed obligations to which he is committed.

It is much more important to have indemnity for long enough periods. Health and accident insurance should be based on need, and should not be carried in excess of that need.

After considerable study of the problem, Professional Management Midwest has adopted the following basic principles regarding health and accident programs.

Amount of Coverage

Monthly coverage should consist of a minimum $400 per month, plus $50 per month for each dependent including the Doctor's wife, and an amount equal to his fixed monthly financial commitments. For example, if a Doctor has a wife, three children and mortgage payments of $150 per month, he should carry at least $750 monthly protection. In making this computation, the physician should make an adjustment for income from outside sources.

Types of Contract

It is our recommendation that at least 50 per cent of the coverage be high-quality, permanent, individual policies with reputable companies. Needless to say, these should be noncancellable and guaranteed renewable to age 65. Thus, at least half of the program will be assured of permanence.

The remaining half of the program should consist of high-grade group contracts. Though semi-permanent, these policies are contingent upon the Doctor's continued membership in the group and on the continuation of the relationship between the group and the insurance company.

Indemnity Periods

Since we believe in long-term catastrophic coverage, as opposed to short-term protection, and since most Doctors have cash and accounts receivable to carry them for at least 30 to 90 days, we recommend the following indemnity and elimination periods.

Sickness: Indemnity should start the thirty-first or sixty-first day, and should be payable for a maximum period of seven to ten years.

Accident: Indemnity should start with the first day of disability and should be payable for life. Since most good policies pay from the first day, no elimination period is recommended.

Health and accident insurance is a highly competitive field, and there are many bad, as well as good, contracts being written today. As with most other goods and services, it should be borne in mind that one gets what he pays for. The day one becomes disabled, it will be too late to discover that he has purchased a virtually worthless policy. Thus, with the aid of his insurance advisor, the physician should carefully evaluate his needs and each contract's provision before he buys.

William D. Huntington*
Minneapolis, Minnesota

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*Northern Division Manager, Professional Management Midwest.

The Relative Value Schedule of Hammurabi

Hammurabi, king of Babylon about 2240 B.C., was famous as a legislator. He developed a code of ethics, laws, principles, consisting of 282 paragraphs which were engraved on a stele* of black diorite* which is now in the galleries of the Louvre in Paris.

Some of the laws with relation to doctors are embodied in paragraphs 215 to 224:

If a physician has healed a man's eye of a severe wound with a bronze instrument or has opened a spot in a man's eye with a bronze instrument and so heals a man's eye, he is to be paid 10 shekels for his work. If the man is a nobleman, the physician will receive 5 shekels of silver and if the patient is the slave of a free man, the master will give the physician 2 shekels.

For a broken limb or for a sick bowel, the patient is to pay the doctor 5 shekels* and if the patient is the son of a nobleman, 3 shekels will be the fee.

If the doctor has been unfortunate and the man's eye is destroyed at the hands of the physician, then the physician's hand is to be cut off.

Editor's Note: I guess we're making progress.

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*See Test Your Word Score Page 763.

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Meetings and Announcements

The more discussion the better, if passion and personality be eschewed. — Discussion, even if stormy, often winnows truth from error. — Channing.

JUNE

Annual Meeting of the Medical Library Association, May 30-June 3; Bellevue-Stratford Hotel, Philadelphia. Contact: Medical Library Association; 919 No. Michigan, Chicago.

American Cancer Society Scientific Meeting, Drake Hotel, June 16, Chicago. Symposium on "Hormones and Chemotherapy for Cancer" is open to all members of the medical and dental professions. Contact: Society, 219 E. 42nd St., New York.

American Physical Therapy Association Annual Meeting, Cleveland, Ohio, June 27-July 2, Sheraton-Cleveland Hotel. Contact: Association, 1790 Broadway, New York.

Southern Minnesota Academy of General Practice, Seminar, 3:45 p.m., June 1, Fairmont.

St. Louis County Medical Society, Executive Comm., 6:00 p.m., St. Luke's Hospital, Duluth, and Regular Meeting, 8:00 p.m., June 10.

Minnesota Dept of Health, Div. of Special Services, 8:30 a.m.-4:00 p.m., Continuation Center, Univ. Campus, Minneapolis, "Handicaps of Premature & New Born," June 10-11.

Minnesota Assoc. for Retarded Children, Annual Conference, Macalester College, St. Paul, June 11-12.

Tuberculosis and Health Association of Hennepin County, Annual Meeting, 12:15 p.m., Capp-Towers, Minneapolis, June 16.

American Medical Association, Annual Convention, New York, June 20-24.

International College of Surgeons Regional Meeting, June 30-July 5, Mont Gabriel, Quebec, Canada. Contact Stanley Henwood, 1516 Lake Shore Drive, Chicago.

Seventh Annual AMA-ASHA Preconvention Session on School Health, June 20, New York City, Contact: AMA.

The Minnesota State Medical Assistant's Society will hold their 2nd annual convention at the Hotel Duluth, Minnesota on June 4, 5 and 6, 1965. Registration will start Friday evening, June 4, at 7 P.M.

JULY

Nineteenth Annual Rocky Mountain Cancer Conference, July 16-17, Brown Palace Hotel, Denver Colorado. Contact: Rocky Mountain Cancer Conference, 1809 East 18th Avenue, Denver, 80218. . .

Zumbro Valley Medical Society — Regular Meeting, July 1, 8:00 p.m., Plummer Hall, Mayo Clinic, Rochester.

Minnesota Surgical Society — Business & Program, July 16. Duluth, "Advances in Pediatric Surgery."

ANNOUNCEMENTS

Hahnemann Medical College & Hospital, Philadelphia, postgraduate courses:

July 26-30 — Interpretation & Therapy of Cardiac Arrhythmias, Hahnemann CVI Bldg., Philadelphia.

Nov. 22-24 — Symposium Cancer Chemotherapy, Sheraton Hotel.

* * *

Three-day course directed to surgically oriented physician will be held at the University of Wisconsin's Medical Center, Aug. 26-28. Aspects of cardiovascular surgery, biliary tract surgery, and general abdominal surgery will be presented. Write: The University in Madison.

* * *

Next scheduled Part I (written) examination by the American Board of Obstetrics and Gynecology will be held at various examining centers on July 2, 1965 at 10:00 a.m. Applications received for next Part II examination to be given in Chicago in April 1966 will be reviewed in September and notification will be mailed October 1st.

* * *

A symposium on Cardiac Emergencies will be held in the anditorium of the Ramsey County Medical Society, Lowry Medical Arts Bldg., St. Paul on June 4 and 5. No fee for registration. Open to all physicians. Laboratory demonstrations will be included as part of course. Sponsored by Department of Medicine, Ancker Hospital, Minnesota Heart Association, State Health Department and St. Paul City Health Department. Contact: James Hammarsten, M.D., Ancker Hospital.

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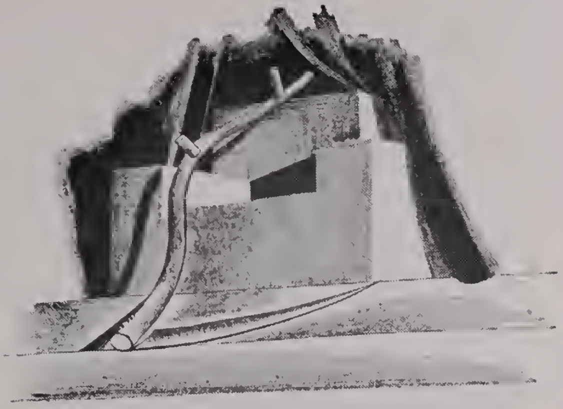
See JAMA May 10 for complete scientific program—forms for advance registration and hotel accommodations.



In Memoriam

Whether your time calls you to live or die, do both like a prince.—Sir P. Sidney

ARTHUR W. GARBRECHT, M.D.

Dr. Arthur W. Garbrecht, 71, St. Paul physician, died April 8th. He was born in Berlin, Germany, and received his degree in medicine from the Friedrich-Wilhelm University in Berlin.

Having practiced medicine in St. Paul since 1924, Dr. Garbrecht was a member of the Radiological Society of North America, a staff member at Riverview Memorial hospital, member of the American Medical Association, Minnesota State Medical Association and the Ramsey County Medical Society.

He is survived by his wife and daughter.

DOROTHY W. HUTCHINSON, M.D.

Dr. Dorothy W. Hutchinson, 66, a physician at Glen Lake Sanatorium for thirty-five years, died April 2nd while vacationing in Florida.

She was a member of the American Medical Association, Minnesota State Medical Association, Hennepin County Medical Society, American Thoracic Society and was active in the Planned Parenthood of Minneapolis.

She is survived by her husband, Dr. Robert W. Browne, a retired dentist.

ROLAND EDWARD NUTTING, M.D.

Dr. Roland E. Nutting, 66, prominent pediatrician and member of the Duluth Clinic, died March 26th. He was born in Clarissa, Minnesota, and received his medical degree at the University of Minnesota.

He was the first Minnesota state chairman of the Child Health Organization of the American Academy of Pediatricians, a past chief of staff at both St. Luke's and St. Mary's hospitals, chairman of the board of trustees of the Duluth Congregational Fellowship, and a member of the American Academy of Pediatrics, the American Medical Association, the Northwestern Pediatric Society, the Interurban Academy of Medicine, the Minnesota Pathological Society, the Minnesota State Medical Association, the St. Louis County Medical Society, the Alumni Association of the Mayo Graduate School of Medicine and Alpha Kappa Kappa medical fraternity.

Dr. Nutting is survived by his wife and two sons.

ADOLPH G. LIEDLOFF, M.D.

Dr. Adolph G. Liedloff, 87, retired Mankato physician, died March 20th. He was born in Mankato and graduated from the University of Minnesota Medical School.

He was responsible for halting the typhoid epidemic in 1908 in Mankato and also served as county health officer and county coroner. Dr. Liedloff was a past secretary of the Minnesota Valley Medical Society and the Blue Earth County Medical Society, a past president of the Blue Earth County Medical Society and past vice president of the Minnesota State Medical Association.

He was a member of the Minnesota Trudeau Society, Minnesota Heart Association, Blue Earth County Public Health Association, American Medical Association, 50 Club and Life member of the Minnesota State Medical Association and a former director of the local district of the Minnesota Department of Health.

He is survived by his niece, Mrs. John Castle, of Delaware.

PHILIP SHOWALTER HENCH, M.D.

Dr. Philip Showalter Hench, 69, former member of the Mayo Clinic staff, world-famous authority on arthritis, pioneer in the clinical use of cortisone and co-winner of the Nobel Prize in Physiology and Medicine in 1950 for his work with that hormone, died in Jamaica, on March 30th. He was born in Pittsburgh, Pennsylvania, and graduated from the University of Pittsburgh Medical School. He became a fellow in medicine in the Mayo Graduate School of Medicine in 1921.

Throughout his life, Dr. Hench received many honorary degrees from colleges throughout the world, and for many years was considered one of the leaders in American rheumatology, being one of the founders of the American Rheumatism Association of which he was a past president. Throughout his lifetime, he was honored by practically every country and organization in the world. His memberships in societies and associations were numerous, and the offices he held were many.

He is survived by his wife, two daughters, and two sons, one of whom is Dr. Phillip Kahler Hench of LaJolla.

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Physician's Diary

He alone has lost the art to live who cannot win new friends. — Sir Weir Mitchell

Dr. H. J. C. Swan, Mayo Clinic physiologist specializing in cardiovascular diseases, and **Dr. Patrick A. Ongley**, Mayo Clinic pediatric cardiologist, received the Susan and Theodore Cummings humanitarian award from U. S. Surgeon General Luther Terry, at the American College of Cardiology's annual meeting in Boston. The Mayo specialists were among fifteen American physicians honored.

* * *

Dr. Wesley W. Spink, University of Minnesota professor of medicine, has been named to a newly formed medical advisory board that will aid the Food and Drug Administration in its safety program for drugs and therapeutic devices.

* * *

Dr. Byron U. Musa was the recipient of the Watson Award, presented annually by the Minneapolis Society of Internal Medicine to a physician in graduate clinical training at the University of Minnesota Medical School.

* * *

Dr. Homer H. Hedemark of Ortonville has been elected a fellow in the International College of Surgeons, and **Dr. Anatol Lysyj** of Minneapolis was installed as a fellow of the American College of Obstetricians and Gynecologists.

* * *

Dr. Clarence W. Moberg of Detroit Lakes has been selected as one of the one hundred outstanding Minnesotans to be recognized with a "Republicans' Care" award. This award is given to persons who have contributed much of their time and energy to meeting human needs and working toward the betterment and growth of the communities in which they live.

* * *

Dr. James C. Cain, consultant in internal medicine in the Mayo Clinic, has been elected a member of the Board of Governors, representing Minnesota, of the American College of Physicians.

* * *

Dr. E. G. Hubin has been awarded the Sandstone County Man of the Year Award by the Chamber of Commerce of Sandstone.

NEW LOCATIONS: **Dr. William Martin**, Duluth internist and cardiologist, has accepted a position in Dayton, Ohio . . . **Dr. Robert Witter** and **Robert Murtaugh** of Wadena have dissolved their partnership and set up individual offices . . . **Dr. Phillip J. Parker** of Staples will practice medicine in Fertile . . . **Dr. E. C. Bayley** and **Dr. D. W. Sontag** plan to construct a new professional medical building in Lake City . . . **Dr. B. R. Briones** of Minneapolis, joined the Drill Clinic of Hopkins.

* * *

Doctors **Keith E. Holley, Andrew G. Engel, Franz J. Hallermann, Leo F. Black, David R. Sanderson, Raymond A. Lee** and **John T. McCall** have been appointed to the staff of the Mayo Clinic, Rochester.

* * *

Dr. Terrell F. Yeager of Anoka has been installed as a Fellow of the American College of Obstetricians and Gynecologists.

* * *

Dr. Arthur H. Bulbulian, director of the Mayo Medical Bureau, will be guest of honor at the fourth annual Banquet of the Golden Plate at Dallas, Texas. The banquet is "A Salute to Excellence" limited to fifty outstanding persons in this country and abroad in the fields of science and humanities.

* * *

The new officers of the Worthington Municipal Hospital are: **Dr. Arthur Amick**, president; **Dr. Edward Seisler**, vice president; and **Dr. B. J. Desai**, secretary-treasurer.

* * *

At the April meeting of the staff of the Glencoe Municipal Hospital the following officers were elected for the coming year: **Dr. C. W. Truesdale**, Glencoe, president; **Dr. John J. Smyth**, Lester Prairie, vice president and **Dr. Donald Navratil**, Glencoe, secretary-treasurer.

* * *

Dr. Tracy E. Barber, Austin, was elected secretary of the Industrial Medical Association at the Association's Fifth Annual Meeting recently in Bal Harbour, Florida.

* * *

Dr. Rafael Fernandez of the Anoka State Hospital medical staff was recently certified by the American Board of Internal Medicine as a diplomate in internal medicine.

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1. Goodgold, J., Use of Nicotinic Acid-Glycine Mixture in Treatment of Peripheral Vascular Disease, Clinical Medicine 7:12 (1960).
2. Gustafson, Jr. et al. Use of Glycine in the Treatment of Peripheral Vascular Disease, Surgery 25:539 (1949).

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WANTED LOCUM TENENS: multi specialty group desires pediatrician for one year. Salary open. Contact — Northwestern Clinic, Crookston, Minnesota.

PRACTICE FOR SALE: North Central Minnesota. General practitioner grossing $60,000 a year. Fully equipped eight room clinic with X-ray. New 32-bed hospital nearby. Reasonable and/or terms. Write: MINNESOTA MEDICINE — 306; 496 Lowry Medical Arts Building, St. Paul, 55102.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE — 289; 496 Lowry Medical Arts Building; St. Paul, 55102.

WANTED: Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty seven bed hospital, X ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact: A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

WANTED: Younger or older general practitioner who is tired of solo practice for association with 15-man midwest clinic in town of 30,000. Two generalists now on staff. We can offer a more comfortable but adequately compensated family practice with accessible consultation and off-time coverage. Write: Herbert H. Kersten, M.D.; Fort Dodge, Iowa.

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WANTED: General practitioner at Kerkhoven, 110 miles west of Twin Cities, approximately 5,000 patient load, fully equipped clinic; two accredited hospitals within 16 miles; new high school; fine churches; excellent farm area at edge of lake country. Contact: Kenneth Peterson, 234-5151, Kerkhoven, Minnesota.

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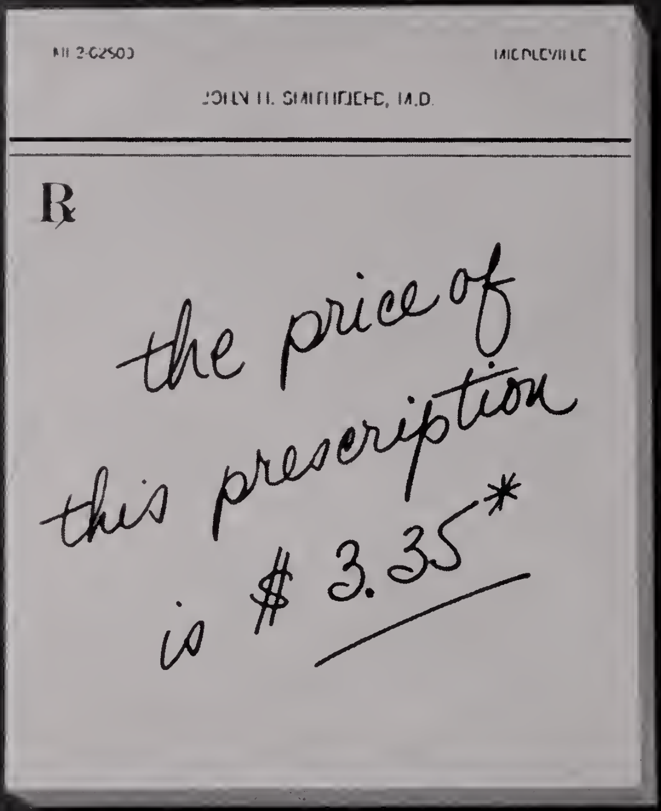

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*Dorhout Mees, E.J., and Geyskes, G.G.: Acta med.scandinav. 175:703,1964.

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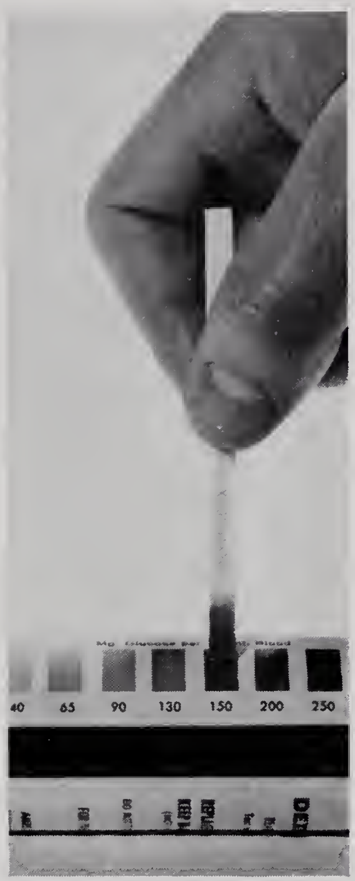

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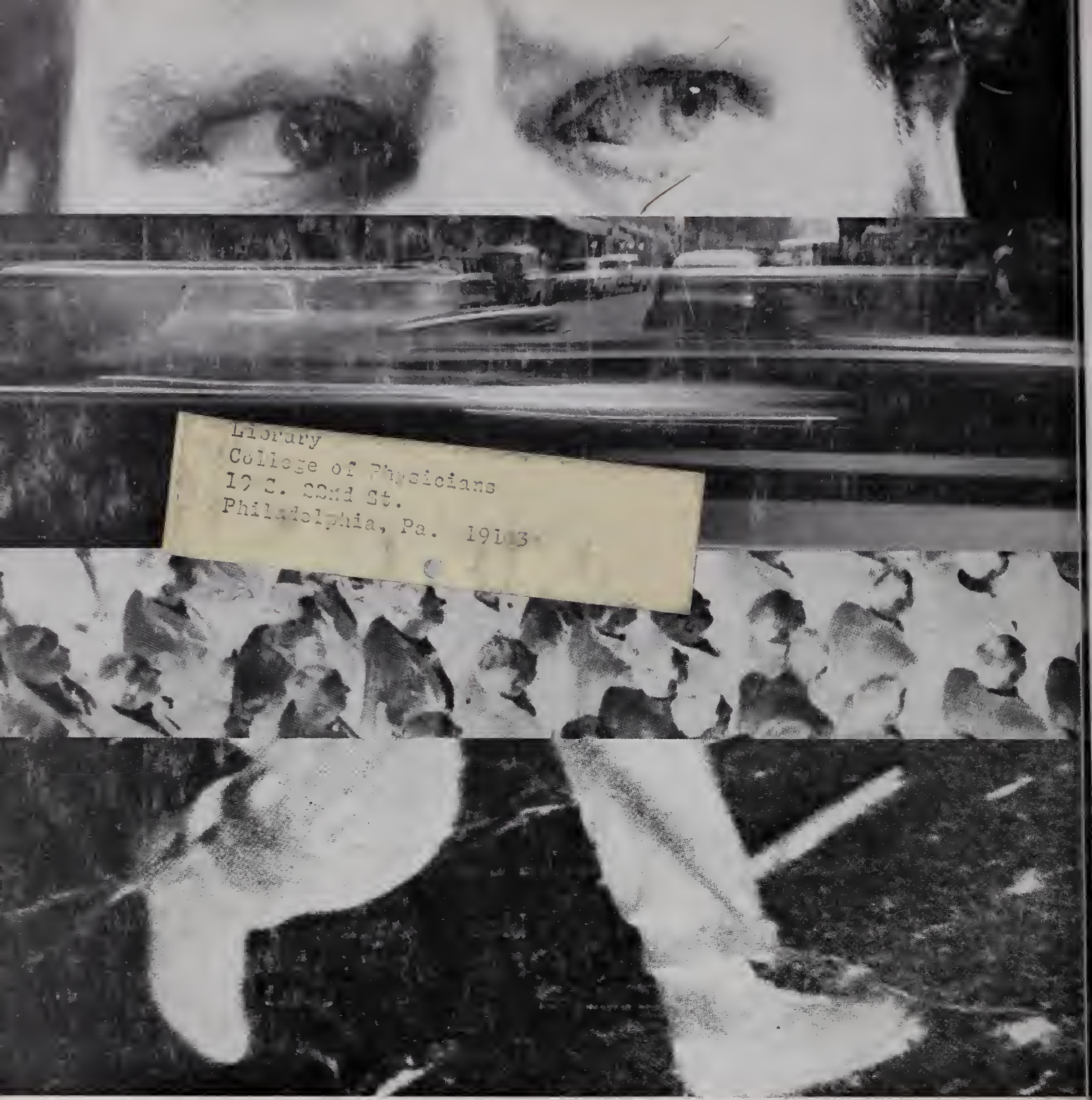

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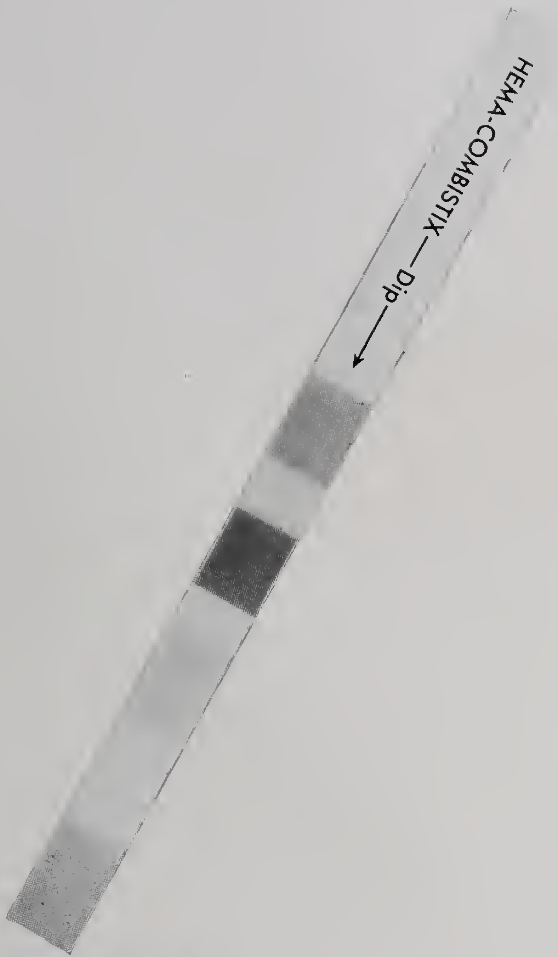

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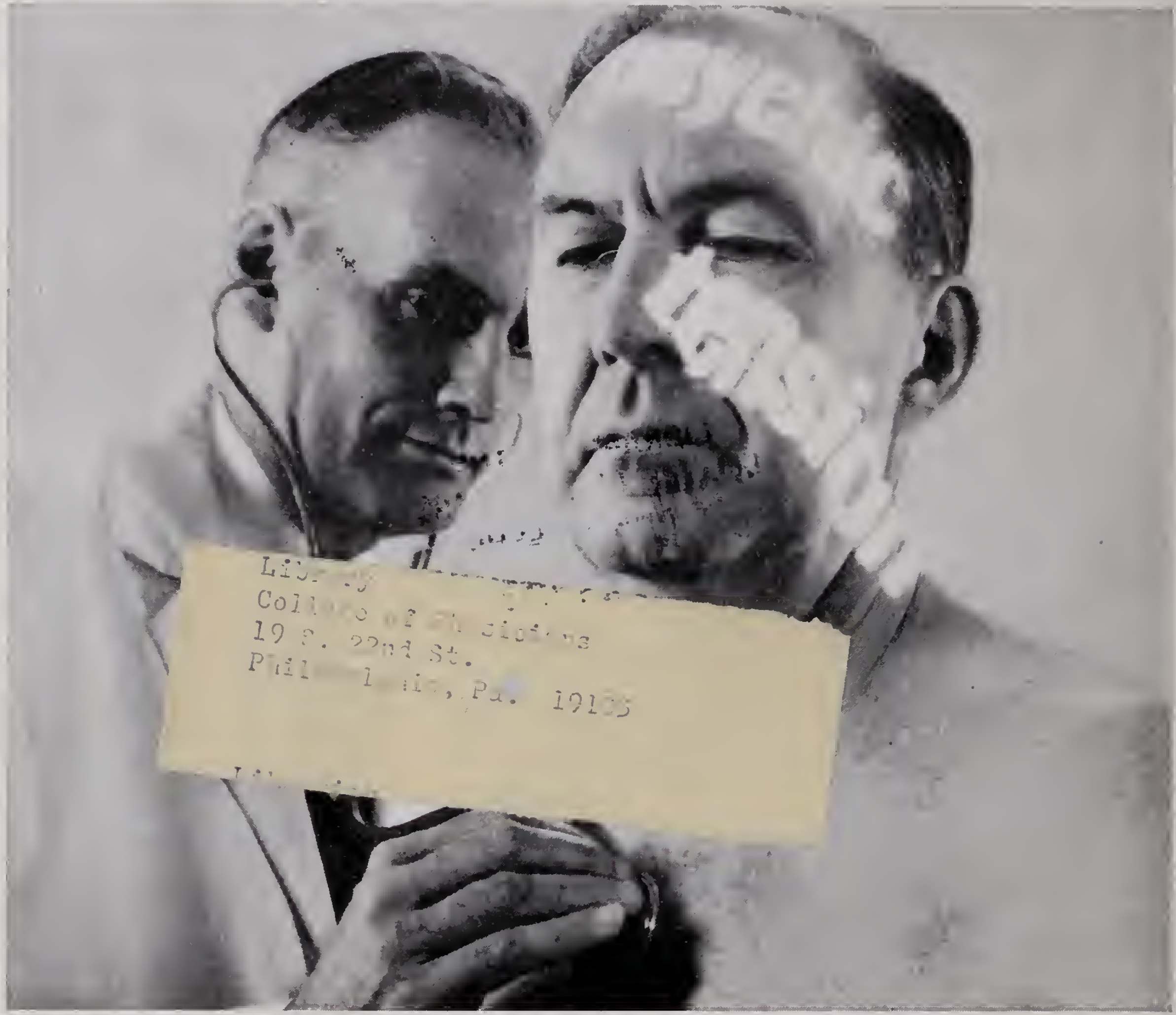

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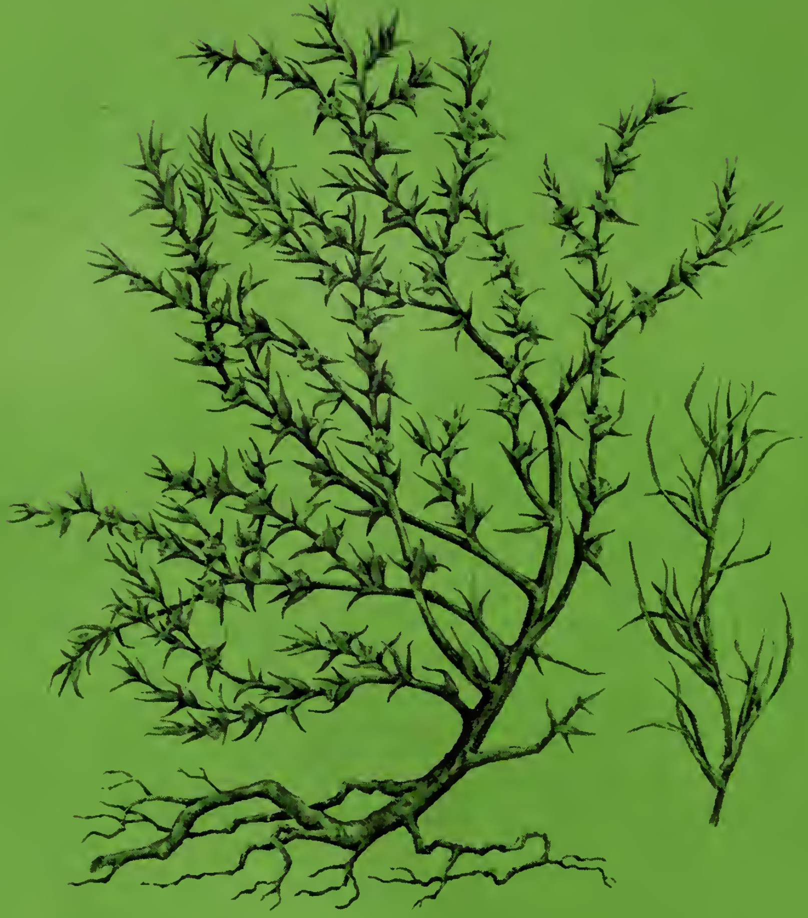

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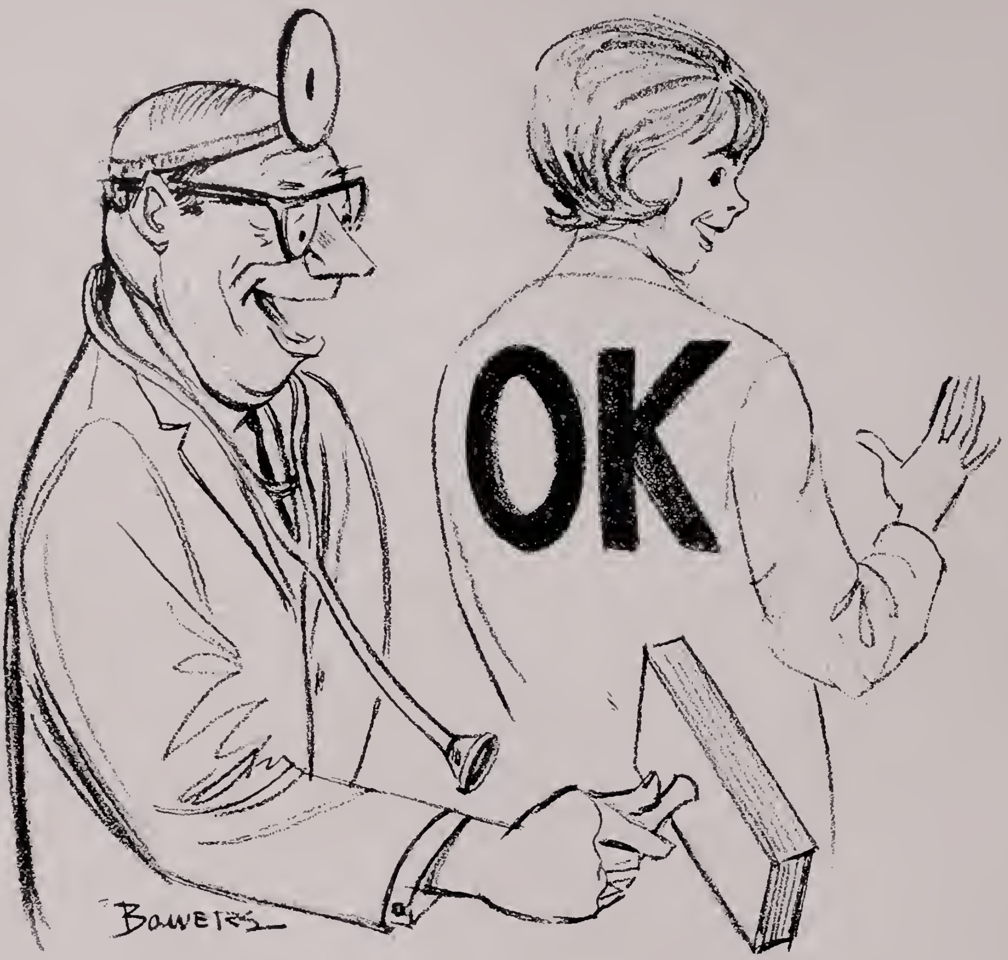

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President's Letter

There is much written and said about the image of the physician in today's society. In an earlier day he was better educated than most of his fellow citizens and was regarded as always available to anyone in distress. Today a greater portion of any community is well educated and the physician may have become less available as he has become more specialized. Polls of opinion, however, show that our profession still maintains a position high in public esteem, although the individual physician may be more highly regarded than the organizations to which he belongs. Many factors such as specialization, group practice, the increased complexity of diagnostic procedures, third party prepayment and insurance plans, and government medicine serve to depreciate or obscure the role of the individual physician. Such trends become more evident as the size of the community increases.

There are two factors in our public relations which are important in maintaining a high level of esteem. The first is ready availability of satisfactory medical care. This can be accomplished by a composite of individual and group action. No propaganda of any type can be as impressive to the patient as the kindly and careful attention of his physician. Patients probably do not expect that each physician will always be at beck and call, but they should know how to obtain satisfactory service outside of regular hours. The unprecedented number of patients appearing at hospital emergency rooms for ordinary care reflects this need. Physicians and the local medical society have an obligation to provide a service organized for good care and made known to the public.

Another facet of good public relations is community service. Working with fellow citizens provides an opportunity to exchange ideas and ideals. I have found that people are more willing to discuss medicine's problems with me when I have served with them in church, chamber of commerce, or United Fund activities. Party workers in either political party will listen more intently to the physician if he participates in the discussion of all issues, not just those of medical interest. Dr. Walter Judd has pointed out that the medical profession is seldom heard from except when its own problems are involved. We should be widely informed and active in community affairs. Most physicians are too busy to participate in many activities but each of us should find time to contribute to a worthwhile endeavor which brings contact with other responsible citizens. There are some who still live and practice in an ivory tower believing that medical service is enough. A community, large or small, thrives on a balanced leadership from all its segments, and medicine should not be unrepresented lest it be misrepresented.

J M Stickney M.D.

J. M. Stickney, M.D.
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Composite Grafts

For Repair of Nasal Losses*

LYLE V. KRAGH, M.D.
Minneapolis, Minnesota

OCCASIONALLY PERSONS sustain losses of ala, tip or columella of the nose that are difficult to repair. Many of these losses are the result of avulsion-type auto or machine accidents or of dog bites. Also, the person whose face is severely burned may lose full thickness substance of the lower part of the nose. Carcinomas of the lower nasal skin may be deeply invasive and require full thickness removal for their eradication, leaving a similar type defect. It must be emphasized that the nasal losses under discussion here are through-and-through full thickness losses, not just of the surface skin.

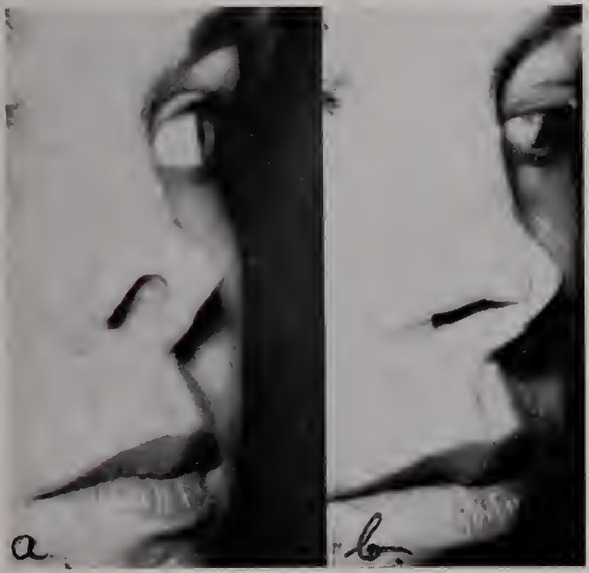

Fig. 1 — *(a)* Traumatic loss of portion of ala and tip of nose. *(b)* Repair of defect of ala and tip utilizing two composite ear lobe grafts. The ear lobe grafts were transplanted to the nose in two operations about five months apart. The patient still requires a small amount of revision of areas about the tip.

Some nasal tip and alar defects can be repaired by a local rotation flap of skin or a pedicle of skin brought to the nose from a more distant part of the body.

The Composite Graft

The method to be presented here is the use of a composite graft (usually taken from the ear) to restore losses about the tip and lower border of the nose.

The composite graft is a free graft which includes not only skin but additional underlying tissue. For repair of defects about the thin rim of the nose, the donor site for these grafts is usually the patient's own ear. Thus these grafts contain skin, subcutaneous tissue and cartilage, if from the helix of the ear; and skin, subcutaneous tissue and fat, if from the ear lobe. From the rim of the helix and from the ear lobe, skin will be present on both surfaces of the graft. These autografts are somewhat similar to the surgically replaced amputated finger tip or the freely transplanted nipple in the reduction mammoplasty.

---

*Presented at the Minneapolis Academy of Medicine, December 21, 1964 .

For the most part, these grafts are used about the columella, tip and ala of the nose. They are thick, with sufficient rigidity and sharpness to restore the contour of the nostril border or to replace most of the entire nostril.

Though these grafts were used successfully on a few occasions in the early part of this century, the large experience in their use came from the military plastic surgical centers during World War II.[3] Brown and Cannon and associates[1,2] at Valley Forge Army Hospital reported on a large number of repairs using composite skin-cartilage grafts from the ear. Dupertius,[6] then at the Philadelphia Naval Hospital, reported on successful similar type repairs using grafts from the ear lobe.

Advantages

The appearance of the healed graft is often quite satisfactory and may be superior to anything that can be obtained with a local pedicle flap of skin. The ear grafts usually match the nose skin well and are not very conspicuous. Also, grafts from the helix or lobe have a very satisfactory shape for use about the ala or nostrils.

Disadvantages

The major disadvantage in the use of free composite grafts is the size limitation for successful take. This thick graft of several tissues must be nourished from the recipient vascular bed, and generally no portion of the graft should be more than one centimeter from the nearest blood supply. In repairing losses about the nostril rim, the graft can be several centimeters long, but the maximum thickness should be about one centimeter or less. Occasionally a large alar defect can be repaired in two or more stages. At the first operation, a large portion of the loss can be replaced and still stay within the safe limits of graft width of about one centimeter. Then at the second operation, several months later, additional grafts can be inserted to correct the remaining defect.

The Technique

The grafts should be transplanted on clean surgical wounds that are free of scar. Hinge-type flaps of nasal skin about the periphery of the defect may be developed which will increase the raw surface and thus increase the size of the vascular bed to nourish the graft. An exact pattern of the tissue requirements is determined by using metal foil. This pattern is then transferred to the ear and a donor site selected to produce a satisfactory graft and to result in as little ear deformity as possible. The graft is then marked on the ear and very carefully cut out. It is handled only with the moistened gloved fingers, avoiding crushing instruments, and is transferred to the nose and sutured in place with very fine sutures. Atraumatic technique in the cutting, transferring and suturing of these grafts is very important for a successful take.

Immediately after the graft is sutured in place, it is pale white, indicating no circulation of red blood cells at that early stage. However, by twenty four hours, and often as early as six to twelve hours, a pinkish tinge may be present in the graft.[7] In most cases, by the second day blood has definitely entered the graft and a good blood supply is established by the fourth day, confirmed by blanching on pressure and return of the pink color on releasing the pressure. The quantity of tissue that must become vascularized and receive nourishment in these thick composite grafts is many times more than in a thin split-thickness or full thickness graft of skin alone.

In most instances of fresh traumatic loss of a portion of the nose, such as a dog-bite avulsion, it is preferable to obtain healing by primary suture or application of a split-skin graft to the area that cannot be closed by suture. Several months later, with a surgically clean wound and under optimum conditions the reconstruction can be carried out with a better chance of success. Immediate repair of alar losses from removal of an epithelioma can often be accomplished satisfactorily with an immediate composite graft.

In these grafts a large block of tissue must receive nourishment from the recipient bed. Increasing the size of the bed by use of a hinge-flap or a tongue-in-groove type graft is helpful.[5] Also, reducing the metabolism of the composite graft by cooling (ice over the dressing or exposure of the graft to air) appears to enhance the chance of successful take.[4]

Ideally, all of the scar tissue should be excised from the base. However, in severe nasal injuries, complete removal of all this scar is impossible. Also the area to be grafted may be an old area of radiodermatitis, a less than optimum situation. The success of the grafts will depend upon the size of block transplanted, the suitability of the recipient's bed and the careful technique with which the graft is handled and sutured in place. With favorable circumstances a success rate of 80-90 percent should be obtained.

Summary

The composite graft is especially useful for correcting defects of the nasal ala, tip and columella that are often not satisfactorily corrected by other methods such as pedicle skin flaps. Relatively large pieces of skin plus cartilage or fat can be transplanted to the nose and will be vascularized rapidly if carefully handled and sutured in place on a surgically clean scar-free bed. With precise technique, a satisfactory acceptance of the grafts should be expected in at least 80 percent of cases. When the grafts are obtained from the ear, the shape and color usually match the nose well and the final appearance is generally satisfactory.

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URETERAL SYNDROME OF LEDUC

LeDuc has indicated that the ureteral syndrome may stimulate acute appendicitis, differing in the fact that the point of maximal tenderness is over the ureteral point instead of over McBurney's point and pain may begin on the right side rather than in the epigastrium, as in appendicitis. The examination indicates there is no rigidity, muscle spasm or rebound tenderness as there is in acute appendicitis.

The location of typical ureteral pain in the male is in either one or both loin or groin along the course of the ureter, and pain may be referred to the external genitalia or into the inner aspect of the thigh. Associated with this there will be urgency of urination as the bladder fills.

Drive Safely

The driver is safer when the roads are dry; the roads are safer when the driver is dry.

Thalamotomy

JIM L. STORY, M.D.
MANFRED J. MEIER, M.D.
SHELLEY N. CHOU, M.D.
LYLE A. FRENCH, M.D.
Minneapolis, Minnesota

THE SYMPTOMS of Parkinsonism can be at least temporarily and partially relieved by stereotaxic neurosurgical procedures. This was originally shown by Spiegel and Wycis.[3,4,6] Subsequent experiences have validated this concept and there are now many patients readily available to verify this. That the procedure is invaluable in the control of the disabling symptoms is beyond question. All patients are not helped by the procedure, however.

The purpose of this report is to present our experiences with lesions produced by the stereotaxic technique in the subthalamic region to control symptoms of this disorder. Our prime effort has been to determine which patients will respond most favorably to surgical treatment. It is true that there is a modicum of difficulty in proper placement of the lesion, but perhaps even more important is the proper selection of patients. These two factors are of equal importance.

Method and Material

A modification of the stereotaxic method of Spiegel and Wycis[4] is utilized to locate the internal reference points, the anterior and posterior commissures, and to place the lesion in the subthalamic region. Localization of the optimal target point is determined radiographically and by physiological method, the latter consisting of a high frequency stimulus applied to the target area with the patient in the awakened state. The stimulus is delivered through a 1.1 mm. diameter concentric electrode which has been passed through a burr hole into the target area. The end point for lesion placement is blocking of tremor in the contralateral extremities for the duration of the stimulus with the least possible amount of current. A 50 to 100-cycle per second, 2 msec. square wave pulse of 0.1 to 0.5 mA or 1 to 5 volts usually blocks the tremor when the optimal target point has been achieved. The stimulating electrode is then replaced by the Bertrand[1] leukotome and the lesion produced. Immediate arrest of tremor and rigidity follows.

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*Inaugural thesis presented to Minneapolis Academy of Medicine, November 16, 1964.

• in • the • Treatment • of • Parkinsonism*

TABLE 1
Results of Thalamotomy in 50 Patients with Parkinsonism

Results	Number of Patients	Percentage of Total	
Good	16	32%	56%
Fair	12	24%	
Poor	22	44%	

Lesions in the subthalamic region have been placed in fifty patients. The experimental studies of Strassburger and French[5] have shown this region to be particularly effective in the control of tremor and rigidity. Postsurgical follow-up of forty-eight of the fifty patients ranges from two to 33 months, with an average of 16 months. Preoperative manifestations of the disease in many of these patients have included, in addition to the typical tremor and rigidity, marked akinesia (poverty of movement), masked facies, and vegetative signs such as flushing, seborrhea and excessive sweating.

The patients have been divided, according to results, into good, fair, and poor groups. The various groups are defined as follows:

Good: a) relief of tremor and/or rigidity
b) over-all functional improvement

Fair: a) some recurrence of tremor or rigidity but less than preoperatively
b) functional improvement subjectively and objectively

Poor: a) no improvement
b) worsened by the procedure
c) temporarily improved but over-all poor because of progression of the disease

Results and Discussion

There were 16 or 32% good, 12 or 22% fair, and 22 or 44% poor results. Combining good and fair, there were 28 or 56% improved (Table 1).

There were no deaths in this group of fifty patients. There was one postsurgical hemiplegia, and four patients developed a mild hemiparesis. Two demonstrated an increase in tremor, and five were considered to have worsened by the procedure.

A review of pertinent clinical variables suggests that operative results are a function of symptom duration and the amount of preoperative akinesia.

Table 2 shows distribution data and significance tests for differences between the groups in duration of symptoms according to number of years. It can be seen that the difference of 10.6 years in duration between the good and poor outcome groups yields a t ratio of 4.09, which is significant at the .001 level of confidence. That is, a difference of that magnitude would not be expected to arise more than once in 1000 comparisons on a chance basis. Similarly, .001 level differences arise when the combined fair and poor groups are compared with the good group and when the combined good and fair groups are compared with the poor group. Thus, a positive relationship between outcome and symptom duration is strongly suggested.

The comparisons between outcome classification and preoperative ratings of akinesia can be seen in Table 3, where the amount of akinesia was rated along a nine point scale: 0, 1, 1+, 2, 2+, 3, 3+, 4, 4+. These ratings were broken down for purposes of analysis into three sectors: Absent (0), Mild (0+ through 1+), Severe (2 or more). The observed and expected frequencies for each outcome group on each sector are located in the nine-fold Chi-square matrix of Table 3. All of the good group exhibited mild or no akinesia, while the poor group was divided, with a preponderance of severe akinesias but none with absence of akinesia. The Chi-square of 19.56 yields a probability of one in 1000 for obtaining the observed frequencies on a chance basis. Similarly, combining the fair and poor groups or the good and fair groups for comparison with the remaining group shows significant deviation from chance expectancy as inferred from the obtained Chi-square values. Thus, the more akinesia* judged to be present preoperatively, the more likely is a poorer outcome to follow thalamotomy in this series of patients.

TABLE 3
Comparisons Between Clinically Estimated Outcomes of Thalamotomy as a Function of Preoperative Ratings of Akinesia

		Outcome		
		Good	Fair	Poor
Akinesia	Absent	7 (2.4)	1 (1.9)	0 (3.3)
	Mild	8 (7.5)	6 (5.6)	8 (9.4)
	Severe	0 (5.6)	5 (4.2)	12 (7.5)

$x^2 = 19.56$ @ 4 degrees of freedom
$p = <.001$

		Outcome	
		Good	Fair + Poor
Akinesia	Absent	7 (2.4)	1 (5.2)
	Mild	8 (7.1)	14 (15.0)
	Severe	0 (5.6)	17 (11.3)

$x^2 = 20.86$ @ 2 degrees of freedom
$p = <.001$

		Outcome	
		Good + Fair	Poor
Akinesia	Absent	8 (4.7)	0 (3.3)
	Mild	14 (12.7)	8 (10.9)
	Severe	5 (9.9)	12 (7.5)

$x^2 = 11.17$ @ 2 degrees of freedom
$p = <.01$

Even though there was no definite history of encephalitis in all patients who had suffered from Parkinsonism for many years, it is our impression that these patients most likely were postencephalitic Parkinsonians. In a number of instances, a definite history was obtained of encephalitis, followed soon thereafter by tremor. One patient related the onset of tremor to encephalitis following a smallpox vaccination. It is our impression that many inflammatory or toxic diseases of the nervous system, often subclinical, may be followed in time by the Parkinson syndrome. It is emphasized that this is a true syndrome, a composite of symptoms, not a

TABLE 2
Significance Tests for Differences Between Clinically Estimated Outcomes of Thalamotomy as a Function of Symptom Duration in Years

	Symptom Duration Means, Standard Deviations and t ratio					
Comparison	$Mean_1$	$S.D._1$	$Mean_2$	$S.D._2$	t ratio	$(N_1 + N_2 - 2)$
$Good_1$ — $Fair_2$	16.5	11.4	10.6	7.3	1.51	23
$Fair_1$ — $Poor_2$	10.6	7.3	5.9	2.3	.79	29
$Good_1$ — $Poor_2$	16.5	11.4	5.9	2.3	4.09***	32
$Good_1$ — $(Fair + Poor)_2$	16.5	11.4	7.6	5.1	3.68***	43
$(Good + Fair)_1$ — $Poor_2$	13.4	10.2	5.9	2.3	4.71***	43

*** = probability $<.001$

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*See Test Your Word Score Page 901.

specific disease entity.

In general from the data presented, the best results are obtained in the following patients: 1) those with illness of long duration, 2) those who are physiologically young, 3) those with good mental status, a good facial expression and lack of vegetative findings and 4) those with minimal akinesia.

Bilateral tremor or rigidity does not preclude good results provided conditions (1) through (4) are satisfied.

Though it is our feeling that the above criteria for selection of patients are generally true, it has been gratifying and surprising at times to obtain considerable improvement in patients who would have been considered fair or poor candidates for surgical treatment. This improvement is usually transient but, even so, most patients believe it is worth while.

Summary

Fifty patients suffering from Parkinsonism have undergone subthalamotomy with 32% good and 22% fair results. Over-all 56% have been improved by the procedure.

The best results are obtained in those patients with illness of long duration, those who are physiologically young, those with good mental status, good facial expression, lack of vegetative findings, and those with minimal akinesia.

Careful selection of patients should yield improved surgical results.

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Resourcefulness of Medicine

Medicine appropriates everything from every source that can be of the slightest use to anybody who is ailing in any way, or likely to be ailing from any cause. It learned from a monk how to use antimony, from a Jesuit how to cure ague, from a friar how to cut for stone, from a soldier how to treat gout, from a sailor how to keep off scurvy, from a postmaster how to sound the Eustachian tube, from a dairy maid how to prevent smallpox, and from an old market woman how to catch the itch insect. It borrowed acupuncture and the moxa from the Japanese heathen, and was taught the use of lobelia by the American savage.—Oliver Wendell Holmes

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More than one woman has been rendered unhappy for the rest of her life, has been lost and dishonored by a man whom she has ceased to love, because he took off his coat awkwardly, trimmed one of his nails crookedly, put on a stocking wrong-side-out and was clumsy with a button. — Quoted by Balzac

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Ignorance is the night of the mind, but a night without moon or star. — Confucius

*The Place of Jesus in the History of Medicine**

Part II

Christianity entered the world as a religion of redemption. The starting point for the man who would espouse this religion was not an awareness of his worth or power, but of his failure, sin, and suffering. The basic preaching of Jesus and his apostles was "repent and believe the gospel." (Mk. 1:15). Repentance put in its simplest terms is that self-awareness in which men admit their sin and their impotence in the face of it; to believe in the gospel meant to have faith in God's healing or redemptive power. This new religion was grounded not in the glorification of human greatness but in the free and frank acceptance of human suffering, illness, and sin. Jesus was called the Savior, in Greek *Soter* or "healer." His redemptive work is repeatedly described by analogy with the work of a physician in curing the ill. Justin, a church father of the second century, wrote: "Like some excellent physician, in order to cure the sick, Jesus examines what is repulsive, handles sores, and reaps pain himself from the sufferings of others. . ."

This new attitude of acceptance and concern for the ill was rooted in the ministry of Jesus himself. Jesus came healing. He did not explain that sickness is health; he called it by its proper name. He also denied that suffering was the will of God, or a direct and personal punishment for sin. (Lk. 13:1-5). Instead, it was the work of Satan and as such to be resisted and eliminated. (Lk. 13: 16). Jesus brooked no interference in his ministry of healing. The work of healing took precedence over even the most sacred religious traditions, such as Sabbath observance. (Mt. 12:9ff).

Jesus brought into western civilization a new attitude of concern and acceptance for the care and treatment of the ill which has found expression in the growth of modern medical care. Without this basic humanitarian concern, not only for man in his greatness and goodness, but also in his frailty, suffering and illness, the powers of science would never have been harnessed to the cure of disease. The future course of scientific medicine will be marked by growing success as long as its practitioners work in the conviction that their endeavor must be dedicated to achieving for man that wholeness which God intended man to have.

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See Minnesota Med 48:346, 1965 for Part I.

Australopithecus**

The specialized human foot makes possible a balanced, erect posture and rapid movement without recourse to an all-fours position. No ape or monkey has the capacity. He may stand erect momentarily, or stagger along for a distance, but his hands are never freed permanently for chores other than locomotion. Similarly, the special development of that mass of muscle centered in the human buttocks makes possible agility and all the turning and twisting and throwing and balance of the human body in an erect position. As the brain co-ordinates our nervous activity, so the buttocks co-ordinate our muscular activity. No ape boasts such a muscular monument to compare with ours; and it is a failure more fundamental than his lack of an enlarged brain.

Regard yourself. Take pride in your hat-size if you will, but it was the specialization of feet and buttocks that made all else possible, and that truly distinguishes you from all other primates, living and dead, with the single exception of australopithecus.—African Genesis—Robert Ardrey

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**See Minnesota Med 48:342, 1965.

*Blood Group Antibodies as They Affect Transfusion Practices**

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Caution is the ever present "key word" in blood transfusion practices.

IN OPERATING a blood transfusion service we are always dealing with an interplay of antigens and antibodies. From an increasing knowledge of the vast numbers of blood group systems and antigens, we can safely say that every time a person is transfused he is exposed to some antigenic factor or factors which his body will identify as foreign, and to which he may build up antibodies.

At any rate, the more transfusions we give, the more important antibody formation becomes, and the more different varieties of antibody formation we shall be able to study. Those who are responsible for a blood transfusion service, therefore, have to learn to live with antibodies, to expect them to turn up, to set up technics to catch them, and be prepared to make a rapid evaluation of the problem in any given case. Can it be handled with the locally available facilities? Or will outside help be needed?

Acknowledging first that unexpected blood group antibodies do turn up now and then, it is worthwhile to start thinking first of all about how much of a problem this is. In other words, is it really anything for the average transfusion service to be much concerned about?

Irregular antibodies occur a great deal more often than most people realize. At our Center in Chicago we investigated 280 immunohematologic problems in 1963. Of these, almost half came from our own hospital, which has 425 beds and where about 3900 transfusions were given in 1963. This does seem rather a lot of antibodies, even though it includes such things as cold agglutinins when they interfere with a crossmatch. It does not, however, include Rh antibodies as usually determined in prenatal testing. In a study reported by Grove-Rasmussen (Transfusion, May-June, 1964) nearly 40,000 antibodies were detected in 20 reference laboratories out of approximately 2,000,000 specimens either referred to them or passing through their hands, including cases of hemolytic disease of the newborn. This makes an overall occurrence figure in this group of somewhere between 1 and 2%. It is my impression that the vast numbers of antibodies never come to light. They lurk on in their possessors and when the occasion for another transfusion or a blood donation rolls around they may or may not be detected.

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Strong Antibodies — High Incidence Factor

It is tempting to say that the really important antibodies from the clinical point of view will be obvious and should require no comment. Unfortunately, this is by no means true as the following case will illustrate.

Case Reports

Case No. 1

Some time ago a 34-year-old woman at another hospital received a unit of blood which had been crossmatched by the night technician and was considered compatible. No adverse effects were reported to the blood bank until a few days later, at which time the blood bank was notified that complete renal shutdown had occurred. Blood specimens from the patient (post-transfusion) and from the donor whose blood had been administered were sent to us. Both were group O, Rh-positive. However, there was major incompatibility between patient and donor, with hemolysis of the donor cells. The patient's serum also reacted with all other panel cells except the patient's own cells. We are thus dealing with a hemolytic antibody to a high-incidence blood factor. Further investigation disclosed that Vel-negative cells were not affected, that all reacting cells were Vel-positive, and that the patient was apparently Vel-negative. Vel antigen can at times be quite difficult to detect, especially in old blood samples. During the investigation, the patient died.

Unfortunately, a pre-transfusion blood sample of the patient had not been saved, so we were not exactly sure of the way the crossmatch may have reacted. However, we surmise that the presence of hemolysis may have been overlooked.

In this case, a clearly demonstrable antibody must have been present. Apparently, for one reason or another, the night technician failed to note the incompatibility. It may well be that the largest single factor involved here was a certain degree of "automatism": the night technician selected blood of the same ABO and Rh type as the patient, set up the crossmatch and expecting it to be compatible failed to note the hemolysis. Many other less tangible factors may have been involved.

Another case will add emphasis.

Case No. 2

In Paris, a young woman bled from an ectopic pregnancy and was given a single unit of uncrossmatched blood as treatment for shock. It was her misfortune to be phenotype p (Tj^a-negative) and of course the unit she received was P_1 or P_2 (thus Tj^a-positive). As with most people of this blood type, she had strong anti-$P+P_1$ antibodies, and she went into renal failure. Blood of type p was needed for dialysis. She was able to get one unit from a sister in France, one from the only available donor in England, one from us in Chicago, and one from Australia. Thanks to this strenuous intercontinental effort she survived and is well today. Here we have one of the known hazards of the use of uncrossmatched blood.

In both of these cases, we were dealing with strong antibodies to high-incidence factors; hence both are statistical rarities. Being a statistical rarity, however, is scant comfort to the person who gets incompatible blood. The moral in each of these cases is obvious. In the first, alertness on the part of the person responsible for a crossmatch must be unremitting, and his attention must always be actively focused on the task at hand. In the second case the hazards inherent in the use of uncrossmatched blood must not be forgotten.

Weak Antibodies

Having concluded that the potent irregular antibodies are important, we may now question whether the weaker ones really matter. This is a much more difficult matter to decide, because whether an antibody appears to be strong or weak or even undetectable may depend on the method used to detect it.

Case No. 3

Quite a few years ago, for example, in another city I had a surgical patient with anemia due to chronic infection. This patient had had many transfusions without a very good response. Looking into the patient's chart later, we noted clinical comments that there was a very poor response to transfusions, even commented on by a consultant hematologist. In the nurse's notes were remarks of chills and headaches after some of the transfusions. These findings had unfortunately not been communicated to the Blood Bank. The crossmatches were compatible in saline and high protein media. Just at that time I decided to improve our crossmatch routine by adding an antiglobulin crossmatch in multiple transfusion cases. A beautiful anti-Fy^a (Duffy) was promptly detected in the patient's serum. Administration of Fy^a-negative blood resulted in prompt improvement, no more shaking chills were experienced, and the consultant hematologist was now satisfied with the clinical response to transfusions.

In a case like this, the clinical transfusion reactions were relatively mild, but the patient received little or no benefit from most of his transfusions. This in turn resulted in unduly prolonged hospitalization, unnecessary additional clinical consultations, considerable worry to the patient, and pure wastage of valuable blood, all of which are both costly and distressing.

The important thing in dealing with these contingencies is to adopt a positive outlook instead of the negative one so frequently expressed. Even the weakest, barely detectable antibody in the patient may prevent this aim from being achieved if blood containing the particular antigen is given: for one thing it may promptly convert the weak antibody to a stronger one, as undoubtedly happened in the Duffy case above. Many cases have been seen and reported in which transfused blood had had a very short survival in the recipient despite the lack of any obvious or severe clinical reaction.

In short, we should try to eliminate from our thinking and from that of our clinical colleagues the idea that such and such a procedure is acceptable because we can "get away with it." If I seem to belabor this point a little, I am not apologizing for it. I do so because I think it is extremely important.

Now let us consider a few particular types of antibodies and see what practical lessons can be derived from them. I will omit technical details and concentrate mainly on the general principles involved.

Cold Agglutinins

Cold agglutinins (those reacting with the patient's own cells at 4° C.) often present a real problem to the crossmatching technician and are one of the most frequent reasons for consultation with the Reference Laboratory. In most such cases, if the specimens are kept warm, there should be no difficulty in crossmatching. However, in case of strong cold agglutinins, especially when they have a wide thermal amplitude, it is easier to work with serum from which the cold agglutinin has been absorbed. This is quite easily accomplished by adding the patient's own cells (oxalated are best) to his serum and incubating at refrigerator temperatures. It may be necessary to do this several times, until the serum no longer agglutinates the patient's cells at cold temperatures. The absorbed serum can then be used for crossmatching and antibody detection tests in the usual way.

I mention antibody detection tests because a cold agglutinin may mask the presence of an irregular cold-active blood group antibody. I recall several cases in which we tested such an absorbed serum and found a strong cold-active anti-P, which had been completely masked by the presence of the nonspecific agglutinin. If we had not detected and identified the anti-P, it could have caused further delay by causing crossmatch incompatibilities, which might even have been disregarded as due to some remnants of nonspecific activity, especially if tested with cells having a weak P antigen.

Autoimmune Hemolytic Anemia

In cases of autoimmune hemolytic anemia, blood typing and crossmatching may again be a problem. Here we have had good results with a titration technic on the major crossmatch, using activated papain, and running a control with the patient's own cells. We test blood units as close as possible to the patient's own group and Rh type, and select for transfusions the ones which demonstrate the "least incompatibility" by titration. In our experience such blood has always been tolerated well, providing it is given slowly as packed cells, and preferably not more than a single unit a day. Of course such blood does not usually survive much better than the patient's own cells, which have a shortened life, and often transfusion is best withheld pending the outcome of therapy specifically directed to the autoimmune process. The one thing that should not be done is to choose blindly a group O, Rh-negative unit, hoping it will do. For one thing, some of these patients have an autoantibody of hr″ (e) specificity; hence most Rh-negative blood will survive very poorly indeed.

Hemolysis

Hemolysis is particularly liable to occur in cases of ABO incompatibility, Lewis, P + P_1 (Tj^a), Vel and some others, but not Rh. Technicians must therefore always be on the lookout for hemolysis, not only in crossmatches, but also on reverse typing and antibody screening.

Undetectable Antibody

Now let us consider the antibody that isn't there when you test for it. By this I mean that a person has been sensitized previously and may have had demonstrable antibodies, but no activity can be demonstrated in the serum at the time of testing. This can best be illustrated by two cases, in one of which a reaction occurred.

Case No. 4

This case was published in the AABB Bulletin in November, 1960, and concerns a middle-aged woman who had been transfused only twice previously. At surgery she received eleven units of blood without ill effects. However, one week later she had nausea and vomiting and hemoglobinuria, followed in a couple of days by jaundice and a fall in the hematocrit. By this time it was discovered that she had a positive direct Coombs test and two antibodies: anti-c and anti-Jk^a. It was evident that she had been sensitized previously, but that the antibodies had dropped in titer to such an extent as to be undetectable by either the antibody screening or the good crossmatching technics used by the hospital concerned. When blood containing the offending factors was given, no reaction took place until the antibody titers had again risen, about a week later, at which time destruction of the transfused cells took place. Fifteen months later, the anti-c had again begun to fall in titer and the anti-Jk^a was undetectable, thus again setting the trap.

Case No. 5

A case was referred to us for a crossmatching incompatibility which on investigation appeared to be due to a mixture of anti-c and anti-K. When this information was conveyed to the referring blood bank director, he had in the meantime found in his files a report from our center, dated in 1958, at which time we reported anti-c and anti-Kidd, not Kell. For some reason we were not able to locate our own file on the patient and were inclined to think that "Kidd" must have been a misprint for "Kell." Nevertheless we tried every trick to demonstrate anti-Jk^a (the patient *was* Jk^a-negative) without the slightest success. At this time, when we were about ready to release apparently compatible c-negative K-negative blood and forget about the Jk^a, we found not only the patient's file, but also 280 cc. of her 1958 serum in our deepfreeze! In the 1958 serum we were able to demonstrate anti-c *and* anti-Jk^a, *and* anti-K. Thus after the 1958 transfusions the Jk^a antibody had disappeared. As it turned out the patient got along without transfusion. However, if we had selected c-negative, Kell-negative, Jk^a-*positive* blood for her, which we had been prepared to do, it is reasonable to assume that either an overt delayed reaction would have taken place or, at best, the transfused cells would have begun to be coated and to disappear after a week or so.

Dosage Effect

Before drawing some conclusions from these two cases, I want to mention one other phenomenon which may have important practical implications. Some antibodies exhibit a definite "dosage" effect. By that I mean that they react better with cells which are homozygous for the antigen concerned. A good example of this is often anti-c, which when weak will sometimes react only with homozygous cells and not with heterozygous Rh_1 cells (CcDee). The important implication of this is that a homozygous Rh_1 person with a weak anti-c may be crossmatched with a heterozygous Rh_1 donor and appear compatible. The administration of such blood, however, may cause a reaction or at least would be followed by very poor survival of the transfused cells.

What conclusions can we draw from these two cases and from the observation of the dosing phenomenon?

Selective Screening of Patient and Donor

Crossmatching Alone Not Sufficient

Although it may seem heresy to say so, it is evident that crossmatching is not the only answer to the determination of compatibility between patient and donor. Screening for antibodies with carefully selected screening cells should be carried out on both patient and donor's serum by appropriate technics. Weak antibodies are perhaps more likely to be picked up this way, using fresh specimens, than by crossmatching, by which time the donor blood samples may be getting old.

Identity of Antibody

Second, once an antibody is detected it should be identified, and blood lacking the corresponding antigen should be selected. It is not sufficient in such cases, other than in emergencies, to rely on crossmatching alone to select "compatible" blood, as I hope the foregoing discussion has demonstrated.

Blood Group Warning Card

Third, once antibodies have been demonstrated, either in a donor or a patient, that person should be given a blood group card, stating the presence and specificity of the antibody as a warning in case of future transfusions. Likewise a patient's hospital record should contain a report of the irregular antibody, plus pertinent comments about special crossmatching methods that might be necessary. We have made it a practice to send out an original and a carbon of the Reference Laboratory report, so that the referring blood bank can have one copy and the other may be put on the patient's chart.

Multiple Transfusions

One final case may be of interest and illustrates a few more important points.

Case No. 6

An elderly man with a bleeding peptic ulcer had had many previous transfusions. A specimen of his blood was sent to us because of crossmatch incompatibilities with many donors. We noted an incomplete antibody reacting only with cells in which c and e were derived from the one chromosome, hence anti-f (the patient was A, Rh_1Rh_1). After some transfusions of f-negative blood, two days later a weak reaction with Rh_2 cells was noted and a positive direct Coombs test, and anti-c anti-E were defined. Checking back on previous donor samples, it was possible to show that the Rh_1Rh_2 samples (f negative and compatible when given) were now demonstrably incompatible, and presumably responsible for his coated cells. Further transfusions were all Rh_1Rh_1, hence compatible. Three days later, six out of 20 homozygous Rh_1 donors were incompatible, another positive direct Coombs test was noted, and anti-Fy^b was defined. A few days later, yet another antibody began to appear, reacting with Rh_1Rh_1, Fy^b-negative cells, but could not be definitely identified. On that indefinite note the patient died.

What do we learn from this case about the problems that may be encountered in multiple transfusions over a short period of time?

A patient who has already demonstrated that he can build up one blood group antibody should be regarded with suspicion as a likely candidate for another antibody.

All blood samples from such cases and the pilot tubes from the donor bloods given should be saved for as long as the patient is still being transfused or likely to be transfused. The fourth edition of the Standards for a Blood Transfusion Service (American Association of Blood Banks, 1963) requires that all samples from both patients and donors be kept for at least seven days after transfusion. In this case (Case 6), having the patient's pre-transfusion blood for comparison and especially for the cell-typing was invaluable. Following several transfusions, a person's circulating cells are no longer his own. By the same token, being able to test the pilot samples of blood already given and previously compatible is extremely helpful in identifying antibodies as they develop. We keep all such specimens for a month and it frequently pays off. In the Vel case previously described, if the original patient specimen had been saved, it might have been possible to find out with more certainty why the crossmatch had been reported as compatible.

Most important of all, when a patient is receiving many transfusions over a period of days, a new specimen for screening and crossmatching must be obtained on the day of each transfusion, as new antibodies can develop with surprising rapidity.

Conclusions

I hope that discussion of these cases has served to emphasize the selected points considered. I have wanted to emphasize certain principles of good hemotherapy as I see them, particularly those points which are less generally known and which tend to be troublesome in routine blood banking, and especially from the point of view of keeping the patient with an antibody from getting blood with the offending antigen. I have concentrated on the practical aspects only, but I would not want to finish without reminding you that every blood transfusion and every donor test is an experiment in immunohematology, and that the lessons acquired in such random testing have frequently been invaluable from the scientific point of view.

Finally I want to stress once more the importance of a positive attitude in blood transfusion. Too often people seem to regard it as a triumph that the patient comes through a transfusion alive and without an obvious reaction. That is certainly fine, but blood is living tissue and transfusion is difficult, hazardous and expensive. We owe it to the patient to make sure he gets the greatest possible benefit, and we have a further debt to the donor that his blood be used in the best possible way.

IT'S THE LAW

Failing to Settle within Policy Limits Imposes Liability for Excess

By failing to settle, within the $10,000 policy limit, a personal injury action for damages arising out of an automobile accident, an insurance company became liable for the entire amount of a $35,000 judgment against the policyholder. Offset against the insurer's liability was an amount of $2,000 which the policyholder had offered to contribute toward a settlement within the limits of the policy. The policyholder was required to pay $2,000 toward the judgment, leaving an amount of $33,000 payable by the company.

In holding the insurance company liable, a federal appellate court relied upon a finding of bad faith on the part of the company in failing to settle the case. The court pointed out that the policy contained a provision requiring the company to defend any such action against the policyholder and look after his interests, as well as its own.

Under his public liability policy with the insurance company, he was covered up to the amount of $10,000 which the company paid to the judgment holder after the judgment was affirmed by the Montana Supreme Court. The policyholder died without having made any payment on the judgment. The judgment holder then filed a claim against the policyholder's estate for the excess of the judgment over $10.000 and brought suit on the judgment against the administrator of the estate.

In affirming the judgments, the appellate court concluded that there was bad faith on the part of the insurance company in refusing to settle.

Prior to trial of the case, the injured party offered to settle for $9,000. The insurance company's highest offer was $5,000. The policyholder agreed to contribute an additional $2,000. The insurance company was adamant.

Editor's Note: Although this decision does not involve professional-liability insurance, there does not appear to be any reason why the decision would not be applicable to that kind of liability insurance. — The Citation Vol. 10, No. 1.

National Farmers Union Property & Casualty Co. v. O'Daniel, 329 F.2d 60 (C.A.9, Feb. 27, 1964)

The Penalty of Overweight

As for food, half of my friends have dug their graves with their teeth.
—Chauncey M. Depew

If I had more time I would have written you a shorter letter. — Voltaire

Transient Vascular Occlusions

in Acute Strokes[*]

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R. L. RYAN, M.D.[**]
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ATTENTION HAS recently been focused on the role of extracranial occlusive disease in patients with cerebrovascular syndromes. Both angiographic and autopsy studies have confirmed a high incidence of atherosclerotic lesions affecting the carotid and subclavian-vertebral systems, and surgical correction of these defects is being carried out in many areas at the present time. There remains, however, considerable speculation regarding the significance of such lesions in the genesis of the stroke syndrome. Such conflicting data as the repeated demonstration of a complete occlusion in one or more of the extracranial vascular channels unassociated with manifestations of a stroke syndrome on the one hand;[1] a high incidence of encephalomalacia without vascular occlusion on the other; and finally, the continued speculation regarding the role of intracranial vascular disease all tend to suggest that extracranial occlusive disease may be a relatively minor factor in the etiology of the stroke syndrome.

The majority of angiographic studies in stroke cases have not been performed early in the course of this acute illness and do not afford us any reliable information concerning possible transient alterations in intracranial vascular structures.[2,4] The following case reports suggest that temporary occlusion of an intracranial vessel may well be a fleeting phenomenon — persisting long enough to result in tissue destruction (encephalomalacia) — then disappearing so that subsequent angiographic and autopsy studies reveal only encephalomalacia without demonstrable vascular occlusion.

Case Reports

Case No. 1

This 63-year-old female had a past history of arteriosclerotic heart disease and in addition, three years prior to admission, had experienced a transient episode of aphasia. On the morning of admission she suddenly developed aphasia and right-sided weakness. Examination revealed her blood pressure to be 108/60, pulse 84 and irregularly irregular. She demonstrated a marked aphasic disturbance and flaccid right hemiplegia. A lumbar puncture was normal. Between 24 and 30 hours after the onset of her symptoms a left carotid arteriogram was performed which demonstrated nonfilling of the middle cerebral artery. Three days later a repeat left carotid arteriogram, utilizing the same parameters of injection pressure, amount of contrast dye, etc., revealed good filling of the middle cerebral artery (Fig. 1 and 2). Clinically the patient demonstrated only a mild improvement at the time of discharge.

Case No. 2

This 70-year-old female had been discharged from the Medicine Service one day prior to her admission to Neurology following an unsuccessful attempt to convert her atrial fibrillation to a normal rhythm.

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[*] This study was supported in part by funds from U. S. Public Health Service Grant NB03364.

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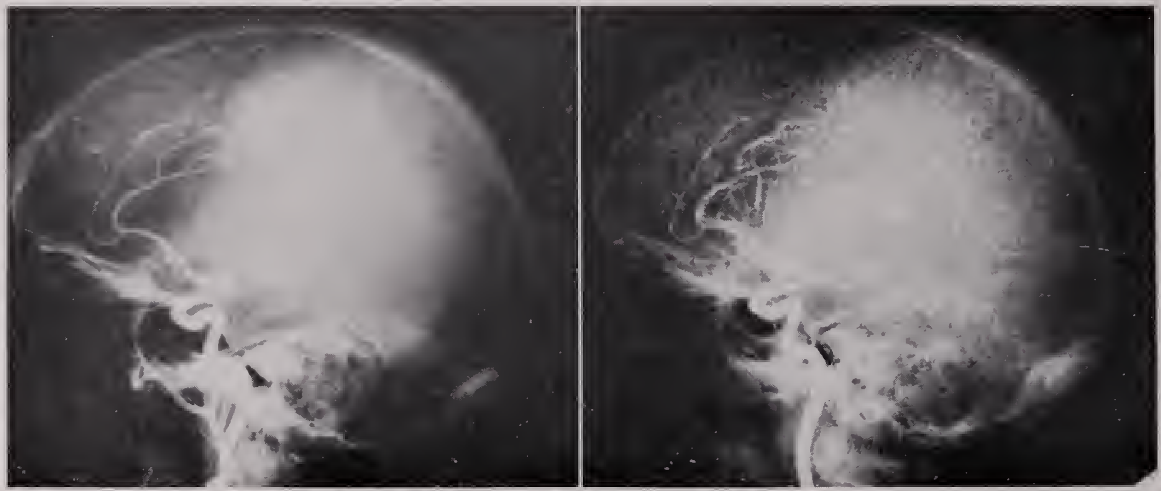
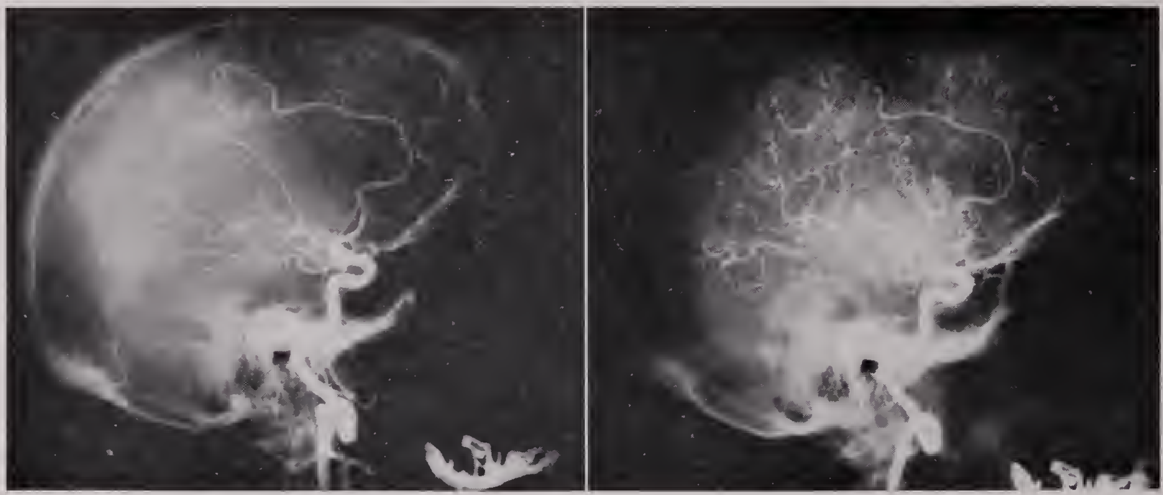


Case 1

24 hours after onset

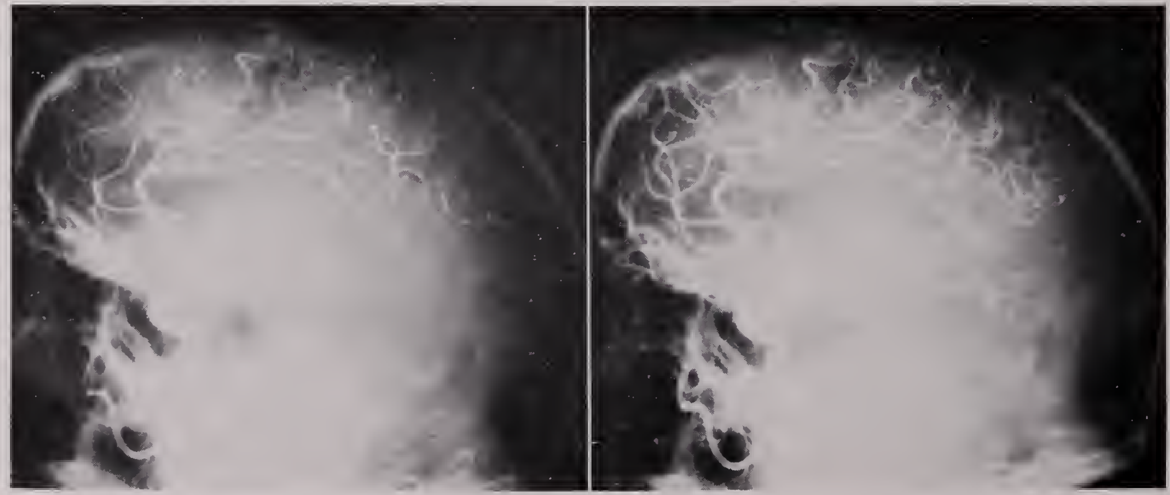
4 days after onset



Case 2

24 hours after onset

4 days after onset



Case 3

14 hours after onset

62 hours after onset

On the day of admission she was found at home, hemiplegic and semicomatose. At the time of initial examination her blood pressure was 160/90, pulse 52 and irregularly irregular. She demonstrated a marked aphasia and right hemiplegia. Her spinal fluid was normal. A left carotid arteriogram performed 24 hours after the onset of symptoms demonstrated occlusion of the sylvian branches of the middle cerebral artery. Three days later a repeat arteriogram revealed filling of the previously occluded segments. Clinically there was little improvement, and the patient was discharged four weeks later with a severe hemiplegia and aphasia (Fig. 3 and 4).

Case No. 3

This 73-year-old male was being followed in the Medicine Clinic for a severe cardiac arrhythmia with a flutter-fibrillation and a variable heart block. On the morning of admission the patient awoke with severe aphasia and right hemiparesis. Blood pressure was 100/60, pulse 72 and markedly irregular. He demonstrated a severe aphasia, right central 7th paresis, mild right-sided weakness, and a conjugate gaze paresis to the right. A lumbar puncture was normal. A left carotid arteriogram performed 14 hours after the onset of the patient's illness revealed nonfilling of the middle cerebral artery. Repeat arteriography 48 hours later demonstrated good filling of the middle cerebral artery. Clinically the patient made a good recovery and at the time of discharge demonstrated only a mild aphasic deficit (see Fig. 5 and 6).

Discussion

We have presented in this report three patients with angiographic evidence of disappearance of an intracranial arterial occlusion. In view of the cardiac dysrhythmias present in all three patients it is our opinion that the most reasonable explanation for the intracranial vascular occlusion is a cerebral embolus. Adams has suggested that in cerebral embolization there is subsequent fragmentation or dissolution of the embolus with its passage on into the cerebral microcirculation after initially occluding a major intracranial artery.[3] There has recently been speculation regarding the role of the naturally-occurring fibrinolytic mechanisms in the dissolution of intravascular occlusions, but insufficient evidence is available at the present time to allow a reasonable appraisal of this problem.

Review of the literature regarding angiographic studies in stroke cases reveals relatively few reports of angiograms performed within the first few hours or days after the onset of the acute stroke syndrome. Eiken, in a survey of 156 patients with strokes, examined 84 cases within the first seven days of onset but does not assess this group of patients separately from those evaluated at a later date.[4] He noted complete occlusion of the internal carotid in 25 cases and branch occlusion of the middle cerebral in eight additional cases. Fifteen instances of severe partial stenosis of a major intracranial artery were demonstrated, and atherosclerosis in the neck vessels was present in 86 of 156 patients studied. In a report of 152 patients with a diagnosis of stroke studied by bilateral carotid and vertebral arteriography, Meyer reports an approximately equal incidence of abnormalities in the carotid-middle cerebral system (315 abnormalities) and in the subclavian-vertebralbasilar system (303 abnormalities).[5] Approximately one half of the carotid arterial lesions were obstructive; of these, two thirds were extracranial and one third intracranial. Occlusion of the carotid artery in the neck occurred in ten patients (6.6%). No information can be extracted regarding relationship of time of angiography and time of onset of the stroke syndrome.

Conclusion

We would urge that the significance of atherosclerotic lesions in the neck vessels of patients with a stroke be evaluated with care. It is certainly conceivable that in some instances a 70-90% narrowing of a vessel lumen or a combination of scattered occlusive lesions might result in sufficient impairment of blood flow to part of the brain to result in a stroke syndrome. On the other hand, an equally attractive theory is that even a relatively small atherosclerotic plaque might serve as the site of a platelet and/or fibrin thrombus, which may then embolize into the distal intracranial circulation. We would, on the basis of our studies, suggest that failure to demonstrate intracranial vascular disease by arteriography or at autopsy in patients with encephalomalacia cannot preclude the possibility that for some period of time preceding the angiogram or the autopsy there did indeed exist an intracranial vascular occlusion of sufficient size or of sufficient duration to result in encephalomalacia.

Addendum

Following the preparation of this manuscript, similar reports concerning transient intracranial occlusions were published by P. F. Bladin in Radiology 82:615, 1964, by P. M. Dalal in Lancet 1:61, 1965 and by Zatz and Iannone in Neurology 15:389, 1965.

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July—Saint Camillus de Lellis

In 16th century Italy Camillus founded a diligent and dedicated order known as Fathers of a Good Death, the members of which cared for the sick both in hospitals and at home. Legend has it that Camillus suffered most of his life from incurable abscesses on his feet; yet toward the end of his life, at age 64, when he was almost totally disabled, he continued his ambulatory ministrations to the sick even when obliged to crawl part of the way. July 18 is his day.

Famous Amulets

Catherine de Medici wore a piece of an infant's skin as a charm, and Lord Byron presented an amulet of this nature to Prince Metternich. Pascal died with some undecipherable inscription sewn into his clothes. Charles V always wore a sachet of dried silkworms to protect him from vertigo. The Emperor Augustus wore a piece of the skin of a sea calf to keep the lightning from injuring him, and the Emperor Tiberius wore laurel round his neck for the same reason when a thunderstorm seemed to be approaching.

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*Massengill, S. E.: A Sketch of Medicine and Pharmacy, S. E. Massengill Co., Bristol, Tenn.-Va., ca. 1941, p. 31.

A merry heart doeth good like a medicine; but a broken spirit drieth the bones.
— Proverbs 17:22

Liberty lies in the hearts of men and women; when it dies there, no constitution, no law, no court can save it. — Judge Learned Hand

Antagonism of Oleandomycin and Erythromycin

During Testing Against Staphylococci

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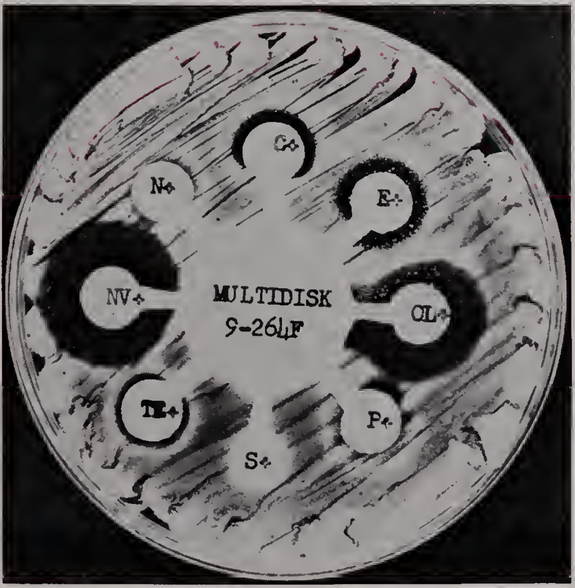

Fig. 1 — Appearance of antagonism between erythromycin and oleandomycin during routine antimicrobial sensitivity studies of staphylococci. Note the flattening of the zone of growth inhibition between the two discs marked E+ and O+.

THE FILTER paper discs which are used at the Minneapolis Veterans Hospital for routine determination of bacterial sensitivity to antimicrobial drugs** are arranged with those for oleandomycin and erythromycin adjacent to each other. One of the authors (M.N.) observed that certain cultures of staphylococci appeared to grow better in the zone between these two discs than in the rest of the area, thus flattening the circle of growth inhibition (Fig. 1).

This finding recalled to memory a report by Garrod,[4] stating that erythromycin and oleandomycin were less effective when used in combination than when employed singly in the treatment of certain resistant strains of staphylococci. In dealing with sensitive strains of staphylococci Elliott and Hall[3,5] observed that the bacteriostatic effect of oleandomycin was potentiated by erythromycin, and that the combination delayed emergence of resistant strains. In the studies of Elliott and Hall only one strain was more resistant to the mixture than to either antibiotic alone. Oskram[8] reported that the effect of this combination was unpredictable. The present study was undertaken in an attempt to clarify the effect of oleandomycin and erythromycin on staphylococci, singly and in combination.

Methods

The study of bacteriostatic effects of antibiotics employed the paper-strip agar-diffusion method described by Elek[2] and Dye.[1] White blotting paper (Grade A, Bermingham & Presser, New York, New York) was cut in strips of about 9 x 1 cm. for impregnation with oleandomycin and of about 5 x 1 cm. for impregnation with either penicillin or erythromycin. The following solutions were used for impregnation of the paper strips: penicillin G 100 units per ml., erythromycin 500 mcg/ml. and oleandomycin 500 mcg/ml. Penicillin was included as a control, since it is accepted that penicillin and oleandomycin show neither synergism nor antagonism. The degree of susceptibility of each of the 66 strains of staphylococci to penicillin was known.

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It was found convenient to make the antibiotic strips in quantity and to store them in sterile glass petri dishes at —20 C, since it was found that this did not result in an appreciable loss of antibiotic activity, even after several months of this cold storage.

Sixty-six strains of hemolytic, coagulase-positive staphylococci were available in pure culture from the clinical laboratories of the Minneapolis Veterans Administration Hospital over a period of several months. These organisms were grown overnight in beef-heart infusion broth, and this culture was used for heavy inoculation of petri plates with nutrient agar by means of sterile cotton swabs. The strips of blotting paper, which had been saturated with antibiotic solutions and allowed to dry, were laid on the freshly inoculated plates in a constant pattern, as seen in Figure 2. They were inspected after 24 hours' incubation at 37 C. Antagonism of two antibiotics was evident whenever the organism's growth was enhanced at the juncture of two paper strips. Addition of bacteriostatic effect was observed whenever the bacterial growth at the juncture of two strips was reduced beyond the inhibition of a single antibiotic (Fig. 2). Sensitivity studies by the tube-dilution method were done in 35 of the staphylococcal strains. Thirty of these had shown antagonism between oleandromycin and erythromycin by the paper-strip agar-diffusion method, whereas five had not. The tube-dilution sensitivity experiments were arranged as follows: Each organism was inoculated in four rows of tubes of nutrient broth. The first row of nine tubes contained decreasing concentrations of erythromycin; the following nine tubes contained decreasing concentrations of oleandomycin. A third row had decreasing concentrations of equal parts of oleandomycin and erythromycin. A fourth set of tubes also contained both antibiotics but were arranged so that the concentration of erythromycin was decreasing in successive tubes, whereas oleandomycin was increasing. The fourth row of tubes (E′ in Table 2) then contained the following concentrations of the two antibiotics:

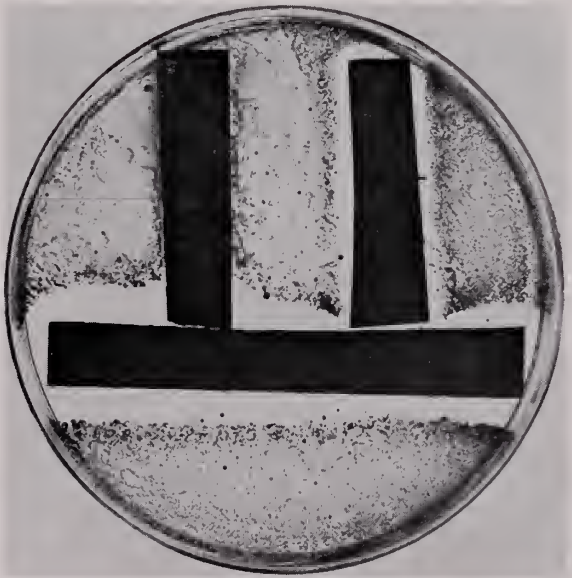

Fig. 2 — Agar diffusion studies. The horizontal paper strip was impregnated with oleandomycin, the vertical strip on the left with penicillin and that on the right with erythromycin. The bacterial growth at the juncture of the erythromycin and oleandomycin-impregnated paper strips is enhanced. There is an additive effect at the juncture of penicillin and oleandomycin.

	Erythromycin	Oleandomycin
Tube 1	50.0 mcg/ml.	0.19 mcg/ml.
Tube 2	25.0 mcg/ml.	0.39 mcg/ml.
Tube 3	12.5 mcg/ml.	0.78 mcg/ml.
Tube 4	6.25 mcg/ml.	1.56 mcg/ml.
Tube 5	3.12 mcg/ml.	3.12 mcg/ml.
Tube 6	1.56 mcg/ml.	6.25 mcg/ml.
Tube 7	0.78 mcg/ml.	12.50 mcg/ml.
Tube 8	0.39 mcg/ml.	25.00 mcg/ml.
Tube 9	0.19 mcg/ml.	50.00 mcg/ml.

The ninth tube dilution in column E′ of Table 2 has been omitted. O′ represents the reciprocal with decreasing concentrations of oleandomycin and increasing amounts of erythromycin, from the ninth to the second tube dilution. All tubes without growth were subcultured on blood-agar plates. When staphylococcal growth resulted, the antibiotic effect in the tube was considered bacteriostatic, whereas a sterile blood-agar plate signified bactericidal effect.

Results

Garrod's observation of varying degrees of resistance of staphylococci to erythromycin could be confirmed. In the case of erythromycin-resistant organisms a gradient zone could be observed at agar-diffusion in which the numbers of colonies decreased with increasing proximity of the erythromycin-impregnated paper strip, leaving a zone of 1-3 mm. immediately adjacent to the strips, which contained few isolated colonies. The same phenomenon was seen in the case of oleandomycin. It was absent in the case of penicillin-impregnated strips. There the colonies either grew right up to the margin of the strip, in the same density as in the rest of the petri dish, or there was a wide margin of growth inhibition which did not contain a single colony. Forty-nine of the 66 strains (76 per cent) showed resistance to penicillin and 34 (51 per cent) were resistant to erythromycin (Table 1).

There seemed to be no relation between the resistance to penicillin and erythromycin. Nineteen strains (29 per cent) were resistant to oleandomycin, and all of these were

TABLE I

Sensitivity of Staphylococci to Erythromycin, Oleandomycin and Penicillin and Incidence of Antagonism between Erythromycin and Oleandomycin, as Demonstrated by Agar Diffusion

Strain of staphylococci		Sensitivity to		Incidence of antagonism between erythromycin and oleandomycin Oleandomycin plus	
	Oleandomycin	erythromycin	Penicillin	Erythromycin	Penicillin
1	S	R	R	A	O
2	S	R	R	A	O
3	S	R	R	A	O
4	S	R	R	A	O
5	S	R	R	A	O
6	S	R	R	A	O
7	S	R	R	A	O
8	S	S	R	O	O
9	S	S	R	O	O
10	S	R	R	A	O
11	S	R	R	A	O
12	S	R	R	A	O
13	S	R	R	A	O
14	S	S	S	O	O
15	S	S	S	O	O
16	R	R	R	A	O
17	S	S	S	O	O
18	S	R	R	A	O
19	S	R	R	A	O
20	S	R	R	A	O
21	S	S	R	A	O
22	S	S	R	O	O
23	S	S	R	A	O
24	S	S	R	O	O
25	S	S	R	O	O
26	S	S	S	O	O
27	S	S	S	O	O
28	S	S	R	O	O
29	S	R	S	A	O
30	S	S	R	O	O
31	S	S	S	O	O
32	R	R	S	A	O
33	R	R	R	A	O
34	S	S	R	O	O
35	S	S	R	A	O
36	S	S	S	O	O
37	R	R	R	A	O
38	R	R	R	A	O
39	S	S	S	A	O
40	S	S	R	O	O
41	S	S	R	O	O
42	S	S	R	O	O
43	S	S	S	A	O
44	R	R	R	A	O
45	S	S	S	O	O
46	S	S	R	O	O
47	R	R	R	A	O
48	S	S	R	O	O
49	R	R	R	A	O
50	S	S	S	O	O
51	S	S	R	O	O
52	S	S	R	O	O
53	R	R	R	A	O
54	R	R	R	A	O
55	S	S	S	O	O
56	S	S	S	O	O
57	S	S	S	O	O
58	R	R	R	A	O
59	R	R	R	A	O
60	R	R	R	A	O
61	R	R	R	A	O
62	R	R	R	A	O
63	R	R	R	A	O
64	R	R	R	A	O
65	R	R	R	A	O
66	R	R	R	A	O

S = Sensitive	A = Antagonism by agar diffusion
R = Resistant	O = No evidence of antagonism

also resistant to erythromycin (Table 1). Antagonism between erythromycin and oleandomycin by the agar-diffusion method was observed in 39 strains (59 per cent), which included all of the 34 erythromycin-resistant ones. By Dye's criteria there was no instance of synergism between oleandomycin and either erythromycin or penicillin. Only three (strain #23, 35 and 37) of the 30 strains which showed antagonism between erythromycin and oleandomycin by the agar-diffusion method failed to show evidence of this phenomenon by the tube-dilution method. Strains 7, 39 and 21, which were only moderately resistant, showed no inhibition when equal parts of erythromycin and oleandomycin were used, but showed some inhibition when the relative amounts of the two antibiotics were varied. There was little evidence of additive effect, as evident in Table 2 by comparison of column B (equal amounts of erythromycin and oleandomycin) with column E (erythromycin) and O (oleandomycin). Interestingly, the antagonism was most obvious in those strains which were relatively resistant to erythromycin but sensitive to oleandomycin. The five strains which did not show antagonism by agar diffusion also failed to show it by tube dilution.

Discussion

These experiments confirm previous observations by others[3,4,6] of the superior effectiveness of erythromycin over oleandomycin against susceptible strains of staphylococci. Resistant strains often showed this quality against erythromycin as well as oleandomycin, but there was no complete cross resistance as observed by others.[7] Twenty-one strains showed greater resistance to erythromycin than to oleandomycin, and it was this particular group which showed antagonism between erythromycin and oleandomycin. Three strains (strains 7, 10 and 43) showed approximately equal sensitivity to the two antibiotics, whereas six showed greater resistance to oleandomycin than to erythromycin (strains 19, 21, 23, 35, 37 and 39). Antagonism between erythromycin and oleandomycin was absent in six strains of staphylococci, which were sensitive to both drugs. One of them (strain 35) had shown antagonism on agar diffusion but not by tube dilution; the remaining five (Table 2-b) were in good agreement

TABLE 2
Effects of Erythromycin, Oleandomycin and Combinations of These Two Drugs in Varying Relative Concentrations on Staphylococci, by Broth-tube Dilution

Staphylococci Whose Agar-diffusion Assays had Shown Antagonism Between Erythromycin and Oleandomycin

Tube No.	Staph. Strain No.																																		
	3					4					5					6					7					10					11				
	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'
1		s			s	C	C	C	C	C		C	s	s	C	s				s	C	C	C	C	C	C	C	s	s	s	C	C	C	s	C
2		s			s	s	C	s		s		C	s	s	C	s					C	C	C	C	C	C	C	s	s		C	C	C		
3		s				s	C					C				s					s	C	C	C	s	s	C	s			s	C	C		
4		s					s					C				s					s	C	C	C	s	s	s	s				s	s		
5		s										s				s					s	s	s	C	C		s	s				s			
6												s											s	s	C										
7																								s	C										
8				s					s					C	s									C	C					s					

Tube No.	Strain No.																																		
	12					13					16					18					19					20					21				
	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'
1	C	C	C	s	C	s	C	s		s		s				C	C	C	C	C	C	C	C	C	C	s	C	C	C		C	C	C	C	C
2	C	C	C			s	C	s				s				s	C	s	s		C	C	C	C	s	s	C	s			C	C	C	C	s
3	s	C	C			s	C	s				s					C				C	C	C	C	s		C				C	C	C	C	s
4	s	C	s				s					s					s				C	s	C	s	s		s				C	s	C	s	s
5		s					s														C	s	s	s	s						C	s	C	s	s
6		s																			C		s	s	C						s		s	s	s
7																							s	s	C						s		s	s	C
8																				s			s	s	C								s	s	C

(Table 2 continued)

	Strain No.																																		
	23					29					33					35					37					39					43				
	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'
1	C	s	C	C	s		s					C			s	C	C	C	C	C	s		s	s		C	C	C	s	C	C	s	C	C	s
2	s	s	C	s	s		s					C				C	C	C	C	C	s		s	s		s	C	C	s	s	C	s	s	s	s
3	s	s	s	s	s		s					C				C	s	C	C	C						s	s	C	s	s	C	s	s	s	s
4	s	s	s	s	s							s				C	s	C	C	C						s	s	s	s	s	s	s	s	s	s
5	s		s	s	s											C	s	C	C	C						s		s	s	s	s	s	s	s	s
6	s		s	s	s											s		C	C	C						s		s	s	s	s	s	s	s	s
7	s		s	s	s											s		s	C	C						s		s	s	s	s	s	s	s	s
8				s	s											s		s	C	C									s	s	s		s	s	s

	Strain No.																																		
	44					47					49					53					54					61					62				
	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'
1		s					s					s			s		s			s	s	C	s		s		s			s		s			s
2		s					s					s			s		s				s	C			s		s					s			s
3		s					s					s					s				s	C					s					s			
4												s					s					s					s					s			
5																	s					s					s					s			
6																																s			
7																																			
8																																			

	Strain No.									
	65					66				
	E	O	B	E'	O'	E	O	B	E'	O'
1		s					s			s
2		s					s			
3		s					s			
4		s					s			
5										
6										
7										
8										

Staphylococci Whose Agar-diffusion Assays had not Shown Antagonism Between Erythromycin and Oleandomycin

	Strain No.																								
	8					9					14					15					17				
	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'	E	O	B	E'	O'
1	C	s	C	C	s	C	C	C	C	s	C	C	C	C	s	C	s	C	C	s	C	C	C	C	s
2	C	s	C	C	s	C	s	C	C	s	C	s	C	C	s	C	s	C	C	s	C	s	C	C	s
3	s	s	C	C	s	C	s	C	C	s	C	s	C	C	s	C	s	C	s	s	C	s	C	C	s
4	s	s	s	C	s	C	s	C	C	s	s	s	C	C	s	s	s	s	s	s	s	s	C	s	s
5	s	s	s	s	s	s	s	C	C	C	s	s	s	s	C	s	s	s	s	s	s	s	s	s	s
6	s	s	s	s	C	s	s	C	s	C	s		s	s	C	s		s	s	s	s		s	s	s
7	s		s	s	C	s		s	s	C	s		s	s	C	s		s	s	s	s		s	s	C
8			s	s	C			s	s	C	s		s	s	C	s			s	C				s	C

The twofold dilutions were arranged as described under "Methods":

E signifies twofold dilutions of erythromycin from 50.0 mcg/ml. to 0.39 mcg/ml.

O stands for the same dilutions of oleandomycin

B contains equal amounts of erythromycin and oleandomycin, from 50.0 mcg/ml. each to 0.39 mcg/ml. each

E' contains erythromycin decreasing in twofold dilutions as under E, but oleandomycin increasing twofold from 0.19 mcg/ml. to 50.0 mcg/ml.

O' contains oleandomycin decreasing in twofold dilutions as under O, but erythromycin increasing twofold from 0.19 mcg/ml. to 50.0 mcg/ml.

The readings of each tube are reported as follows:

Blank spaces signify uninhibited growth.

s signifies bacteriostatic effect.

C denotes bactericidal effect.

with the agar-diffusion assay. There was only one sensitive strain, the culture of which was associated with a moderate antagonism between the two drugs (strain 43). The rest of the sensitive strains showed no antagonism.

The antagonism between oleandomycin and erythromycin, demonstrated in this series, had been seen to a much lesser degree in a previous investigation at this hospital.[3] The discrepancy may be due to a difference in the staphylococcal strains which were employed in the two studies. Most of the staphylococci in the study by Elliott and Hall[3] were sensitive to the two antibiotics, whereas the organisms of this series were preponderantly resistant to these drugs. The association of "antagonism" of erythromycin and oleandomycin does not then seem to be a phenomenon due to properties of the two drugs but rather to a quality of resistant staphylococci. Staphylococci resistant to erythromycin may elaborate a product which inactivates these structurally similar antibiotics. It is not likely to be penicillinase or chloramphenicolase, since this "antagonism" between erythromycin and oleandomycin is not present in association with staphylococci which are resistant to penicillin but sensitive to erythromycin. Perhaps this substance only binds these drugs. At this juncture one remembers the unusual protein-binding qualities of erythromycin, which, unlike most other antimicrobial drugs, is bound to orosomucoid in the alpha$_1$-globulins.[9]

Further studies have been initiated with the aim of clarification of the mechanism of this "antagonism" between erythromycin and oleandomycin. Meanwhile it should be borne in mind that the described "in vitro" phenomena may not be readily translated to conditions "in vivo."

Summary

In routine disc-sensitivity studies of a clinical hospital laboratory it was noticed that erythromycin and oleandomycin frequently seemed to inhibit each other, when tested against staphylococci.

Systematic studies by paper-strip agar diffusion and broth-tube dilution confirmed the observation.

Resistant strains of staphylococci usually were resistant to both drugs, but there was no complete cross resistance.

The "antagonism" between oleandomycin and erythromycin was seen predominantly in association with strains of staphylococci which showed either complete or partial resistance to one of these drugs, whereas sensitive strains failed to show this phenomenon to a significant degree.

The association of "antagonism" with resistant staphylococci suggests that this phenomenon is not an inherent quality of these two drugs, but is probably a product of resistant staphylococci which inactivates or binds both of these structurally similar antibiotics.

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The Effect of Digitalis on the Electrocardiograms

Following Exercise In Normal Young Males*

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THIS STUDY was conducted on 23 males who were inmates of the Minnesota State Reformatory at St. Cloud, Minnesota. All men were volunteers; their ages ranged from 21 to 27. The purposes of the study were: (1) To evaluate the effects of digitalis on the exercise electrocardiogram, (2) To determine whether any changes would be produced in presumably normal young men, (3) If changes were produced, to note whether they were in any way similar to changes seen in so-called "positive" exercise tests done on people with coronary artery disease.

Materials and Methods

In the tables presented below, the term "ischemic change" indicates that a change was seen which could be confused with changes ordinarily considered significant in positive exercise challenge tests. A "nonspecific change" indicates changes which are

TABLE I
Change with Digitalis — 23 Subjects

	At Rest	During Exercise	After Exercise
Nonspecific	6	6	0
Ischemic	8	11	13
Total	14	17	13

TABLE 2
Average Pulse Rate Changes — 23 Subjects

	At Rest	During Exercise	After Exercise
Normal	78	139	71
On Digitalis	71	128	90
Off Digitalis for 3 weeks	74	134	92

TABLE 3
Pulse Rate Changes in Cases Showing Significant Electrocardiographic Changes — 23 Subjects

	At Rest	During Exercise	After Exercise
Normal	80	139	91
On Digitalis	73	129	94
Off Digitalis for 3 weeks	75	142	96

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*This work was done under the auspices of the Cardiac Work Evaluation Unit of the Minnesota Heart Association which extends its appreciation for the co-operation of the State Reformatory at St. Cloud, Minnesota.

not diagnostic of those seen in coronary artery disease (T-wave and ST configuration changes which would not satisfy commonly accepted criteria of a positive exercise tolerance test).

During the entire six-week period of testing these men carried on their usual dietary programs and activities (including recreational football). A physical examination, a resting electrocardiogram and a 40-trip exercise test were done on each subject. During exercise a telemetered electrocardiographic monitoring of the V4 lead was carried out, followed by a post-exercise electrocardiogram.

Following this test each subject was given digitora, 1.28 grains (one CAT unit) per ten pounds of body weight over a three-day period, followed by a maintenance dose of one CAT unit daily. Three weeks after digitalization the subjects were re-examined and the previously described procedures repeated.

Digitalis was then stopped, and three weeks later the tests were repeated in an identical manner.

There was no significant subjective evidence of any digitalis toxicity. There was also no significant change in body weights during the entire six-week testing period, which would confirm the absence of any significant gastrointestinal complaints.

Results

(1) Of 23 subjects tested, one exhibited a positive electrocardiographic response to exercise before digitalis was administered.

(2) As can be seen from Table 1, 14 of the 23 subjects showed some change on their resting electrocardiogram after administration of digitalis. During the actual exercise period 17 of 23 showed changes, and following exercise 13 of the 23 showed changes.

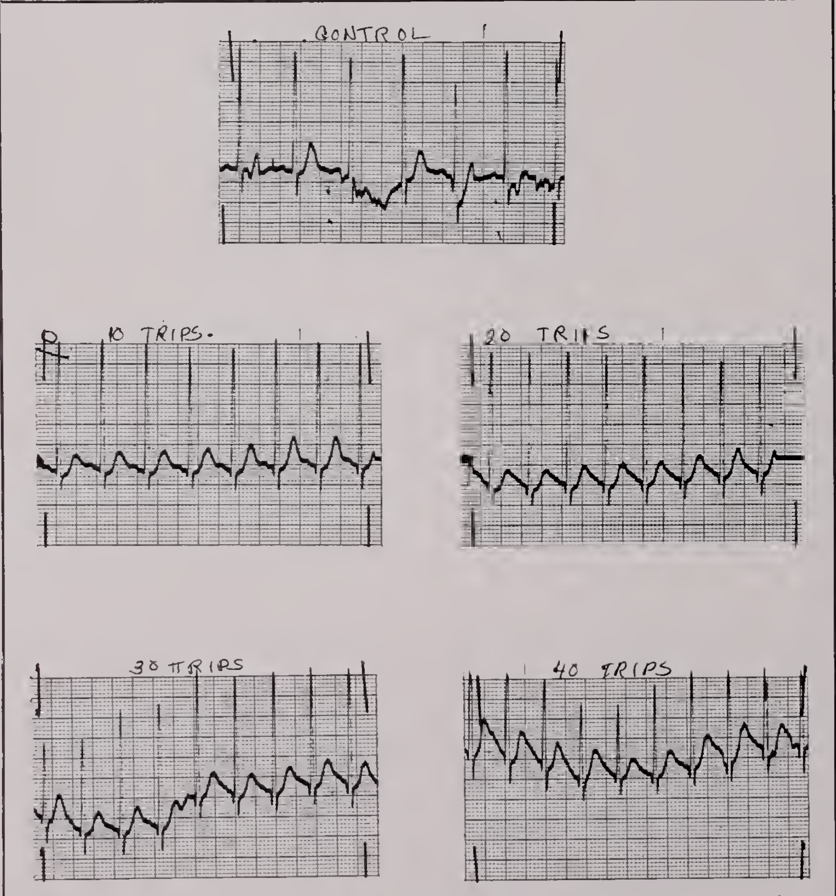

Fig. 1 — *(a)* Telemetered electrocardiogram taken during exercise prior to the administration of digitalis (V4 lead).

(3) In 10 subjects, changes were seen at the final examination three weeks after they had been off digitalis. Of these 10, seven were ischemic in nature and three were nonspecific in nature.

(4) As can be seen in Table 2, there was a significant increase in the average pulse rate during and following exercise. After exercise it returned promptly to the resting rate or below, indicating the basic circulatory integrity of the subjects tested. On digitalis the increase in rate was less pronounced; however, the average rate was initially slower and, in general, did not return to the resting state as promptly as in the control experiment. Three weeks after discontinuance of the digitalis, there was still a significant increase in rate during exercise and the post-exercise rate did not return to the pre-exercise rate.

(5) Considering the possibility that the electrocardiographic changes seen on digitalis may possibly have been related to rate, those patients who showed these changes on digitalis were evaluated with respect to rates as shown on Table 3. As can be seen, there is no significant deviation in this group from the total group.

Comment

It is apparent from these results that significant changes occur on both rest and exercise electrocardiograms following the administration of digitalis. In a remarkably large numer of instances, these changes are indistinguishable from the changes ordinarily associated with a positive exercise tolerance test (see Figure 1). It is also of significance that the changes persist up to at least three weeks following discontinuance of the digitalis in a significant number of cases. It

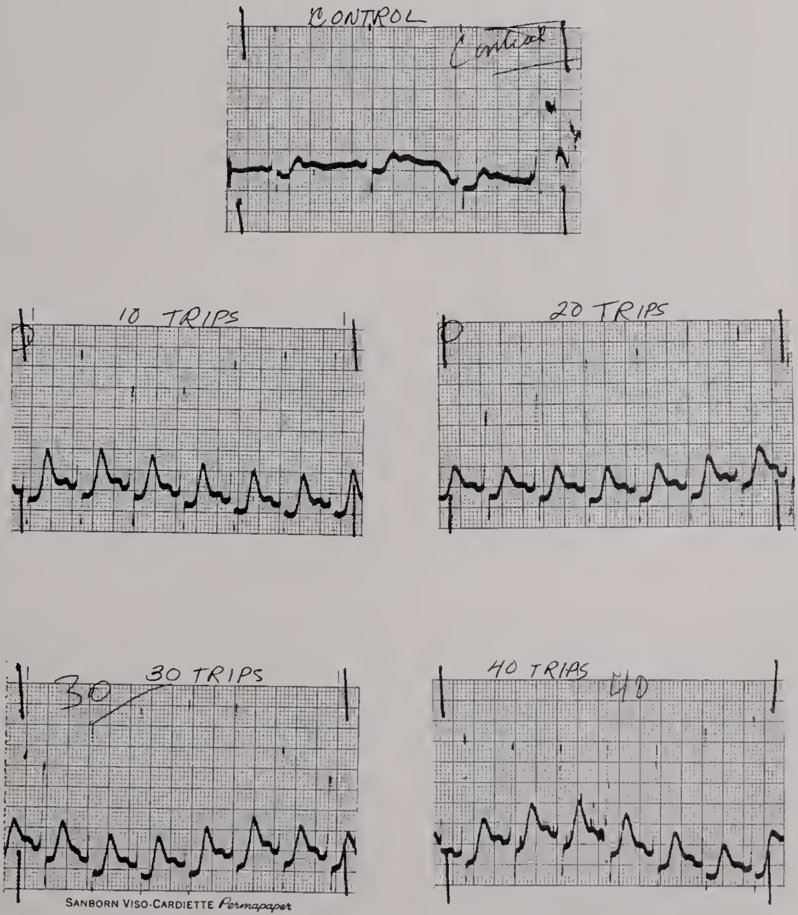

Fig. 1 — *(b)* Telemetered electrocardiogram taken after digitalis.

would seem that interpretation of an exercise test done on a person taking digitalis would be inconclusive because of the identical nature of the changes seen in presumably ischemic exercise electrocardiographic patterns and those patterns seen after the administration of digitalis in the absence of ischemia.

Conclusion

23 volunteers were studied to determine the effect of digitalis on the exercise electrocardiogram. A significant number of subjects showed changes which could be readily confused with those commonly attributed to coronary artery disease when subjected to electrocardiographic exercise tests.

Julian Huxley's Evaluation of Our Makeup*

"Our general construction is determined by the fact that we are made of living matter, must accordingly be constantly passing a stream of fresh matter and energy through ourselves if we are to live, and must as constantly be guarding ourselves against danger if we are not to die." Huxley analyzed us in the following manner, using approximate values:

5%—"consists of a tube with attached chemical factories, for taking in raw materials in the shape of food, and converting it.
2%—"consists of windpipe and lungs — for getting oxygen into our system . . . to burn the food materials and liberate energy.
10%—"consists of an arrangement for distributing materials — the blood and lymph, the tubes which hold them and the pump which drives them.
5%—"is devoted to dealing with waste materials — the kidneys and bladder . . . the lungs and skin.
40%—"is machinery for moving us about — our muscles.
20%—"is needed to support us and to give us mechanical leverage — our skeleton and sinews.
1%—"is set apart for giving us information about the outer world — our sense organs.
3%—"deals with the business of adjusting our behaviour — the ductless glands, the nerves, the spinal cord and the brain.
1%—"is set aside for reproducing the race.
7%—"is concerned with special functions like protection — the skin and some of the white blood corpuscles; or temperature regulations — the sweat glands.
10%—"consists of reserve food stores — fat."

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*A Treasury of Science, 3rd Ed., Harper & Brothers, New York, page 561.

Derivatively Speaking

Digitalis derives from digit (finger) because in German the foxglove from which the drug comes is called Fingerhut (thimble or finger-hat).

Habit is habit and not to be flung out of the window by any man, but coaxed downstairs a step at a time. — Mark Twain

Post Partum Tub Bath

Associated with Morbidity

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THAT A variety of opinions exists regarding the value of routine post partum tub bathing was apparent after a review of this subject.[1] In view of the extensive program of hospital construction at the present time, it would seem important to resolve the question: Should all obstetrical units be designed with tub baths? Architects are constantly seeking advice from obstetricians as to the ideal number and type of bathing facilities required in obstetrical units.

All of us who use the tub bath[2] in the care of post partum patients have stated informally that such tub baths are safe, beneficial, and time-saving. However, an actual clinical analysis of the post partum course of patients receiving tub baths is not available. A study was therefore planned to evaluate the effect on post partum morbidity of a significant number of patients who had received such tub baths. The patients were drawn from the obstetrical services of the Charles T. Miller Hospital, St. Paul, Minnesota, and St. Marys Hospital, Rochester, Minnesota.

Procedure

Charles T. Miller Hospital, St. Paul, Minnesota. — On the first morning after delivery the patient was offered a 15-minute warm, soapy tub bath. This was continued twice daily until the patient was dismissed from the hospital. With this procedure it was possible to dispense with external douches, flushings, bed baths, and perineal lights. Over 20,000 patients have been treated with post partum tub baths by at least 90 per cent of the attending obstetrical staff of the hospital. The opinion of this group of obstetricians confirmed the impression that the procedure is safe. Since 1949, one of us (J. E. H.) has routinely prescribed such tub baths on the first post partum day for more than 3000 private obstetrical patients in the St. Paul area. All case histories since the year 1954 (2150 patients) were reviewed to evaluate morbidity after post partum tub bathing. Fever of 100.4° F. or higher at any time during the patient's hospitalization after receiving a tub bath was considered a sign of morbidity.

St. Marys Hospital, Rochester, Minnesota. — In 1951 post partum tub baths were commenced on a trial basis for the obstetrical patients of the majority of obstetricians practicing at St. Marys Hospital. The obvious benefits to the patient rapidly resulted in the adoption of this procedure as a routine for our normal post partum patients. Originally the baths were permitted on the third post partum morning only. After several years baths were commenced on the second morning and, of late, many patients are permitted baths on the first morning. Many patients are even permitted more than one bath per day.

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Charts of obstetrical patients were drawn at random and reviewed for elevations of temperature after the initial tub bath. Patients whose temperature was elevated above normal prior to the first tub bath were not considered suitable for study. Any oral temperature of 100.4° F. or higher was considered a sign of morbidity. The histories of 10,000 such patients were reviewed personally by one of us (R. A. S.).

Routine

After evaluation of this procedure in both centers, it was evident that a ratio of one tub per six patients was satisfactory.

In both hospitals tubs were prepared in a similar manner. The tub was scoured with an abrasive cleanser, rinsed with water, then washed with green soap and again rinsed. Five or six inches of warm water were drawn. The patient could then sit or lie in the tub, as she wished. The breasts were washed with soap during the bath. All douches, flushes, bed baths and perineal lights were eliminated during the hospitalization. Between tub baths the patient wore a sterile perineal pad.

Advantages of the Procedure

Increase in Patient's Physical Comfort

Physical comfort obviously was improved with elimination of lochia and perspiration from the perineum. The saponific action of the soap dissolves the dried adherent blood and serum from the perineal skin. Analgesics required for perineal discomfort were greatly reduced.

Reduction of Nursing Care

It is estimated that each patient requires at least one to two hours of nursing care per day for the usual and accepted perineal routine. The daily bed baths and series of four to six external flushings require a great deal of nursing time. In contrast, tub baths require less than 10 minutes. Within this time the nurse or aide can thoroughly clean and prepare the tub for the next patient.

Improvement of Bladder Function and Perineal Comfort

The effect of warm baths on improvement of bladder function is well known. The application of this principle to post partum care seems obvious. In the St. Paul study it was noted that the frequency of post partum catheterization was reduced. Reduction of perineal edema and anal discomfort is also noted in the study.

Morbidity

From the study of the 2150 obstetrical patients in the St. Paul area, over-all post partum morbidity was 2.42 per cent or 52 patients. All patients were submitted to tub baths within the first 24 hours after delivery. Of these, 1.58 per cent or 34 patients had fever of 100.4° F. or higher, possibly related to tub bathing; 0.84 per cent or 18 patients had fever considered unrelated to tub bathing.

From the study of 10,000 obstetrical patients delivered in the Rochester area, post partum morbidity was noted in 57 women or 0.57 per cent. Tub bathing was begun in a great proportion of patients 24 to 48 hours post partum. Thirty-two or 0.32 per cent had fever possibly related to tub bathing. Twenty-

TABLE
Causes of Morbidity

Possibly unrelated to post partum tub bathing	St. Paul	Rochester	Possibly related to post partum tub bathing	St. Paul	Rochester
Upper respiratory infection	2	10	Episiotomy infection	4	4
Mastitis (hormonal)	12	14	Endometritis	5	10
Phlebitis	1	1	Urinary tract infection	8	8
Dehydration (diabetic)	1	—	Hematoma	1	—
Toxemia	2	—	Breast abscess	1	—
			Unexplained	15	10
	18	25		34	32

five or 0.25 per cent had fever considered unrelated to tub bathing.

The causes of the post partum fever in the two groups of patients are outlined in the accompanying table.

Comment

In evaluating the post partum patients exhibiting morbidity, the extremely strict criteria for designation of morbidity should be stressed. In both groups all patients who had any temperature elevation to 100.4° F. or higher for any duration of time after receiving post partum baths were included. In spite of this, the percentage of morbidity is exceedingly low.

It should be noted that almost all post partum patients in the St. Paul group received tub baths, in contrast to the Rochester group, in which patients with upper respiratory infections, phlebitis, urinary catheters, post partum hypertension, hemorrhage, or debilitating conditions such as ulcerative colitis were excluded. Another difference in the two series was that patients in the St. Paul group began bathing on the first post partum day rather than the second or third. These two differences probably account for the apparently higher morbidity rate in the St. Paul series. Patients experiencing a brief elevation of temperature, often occurring 12 to 24 hours after the excitement and dehydration of labor, were of necessity included in the latter group, since baths were instituted immediately. In spite of these factors and the strict criteria for morbidity, the rates were extremely low in both groups.

Conclusions

Post partum tub bathing has been evaluated in two representative groups of patients totaling 12,150. The morbidity rate which could possibly be related to the tub bathing was exceedingly low (1.58 per cent and 0.32 per cent). In reply to the question: Should all obstetrical units be designed with tub baths? this study indicates a definitely affirmative answer. In the opinion of staff members of both institutions, a satisfactory ratio is one tub per six patents. Showers are of little use in an obstetrical or gynecological unit. The anatomy of the female is such that the genitalia cannot be adequately cleansed in the shower.

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Tidbits of Medicine

A French drug dictionary quotes these unusual tasty tidbits of medicine that were recommended during the eighteenth century:

Burning hair, smelt by patients, will counteract the vapors. Moss of the human skull, human blood, and human urine all have their uses in medicine. The saliva of a robust young man is an antidote against the bites of serpents and mad dogs. Wax from the ears is good against whitlows. Nails from the fingers and toes, given internally either in substance or infused in wine, make a good emetic. Women's milk is pectoral, good in phthisis, and useful to apply to inflamed eyes. Fresh urine may be applied externally in gout and in skin complaints. Excrement of man can be applied to anthrax, plague bubos, and quinsies. Dried and powdered, it is recommended in epilepsy and intermittent fevers. Dose, one scruple* to a drachm.*,**

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*See Test Your Word Score Page 901.

**Saul, F. William, M.D.: Pink Pills for Pale People. Dorrance & Company, Phil. 1949, p. 64.

Primary Ileojejunal Ulcers

*A Possible Relation to Oral Enteric-Coated Potassium Therapy**

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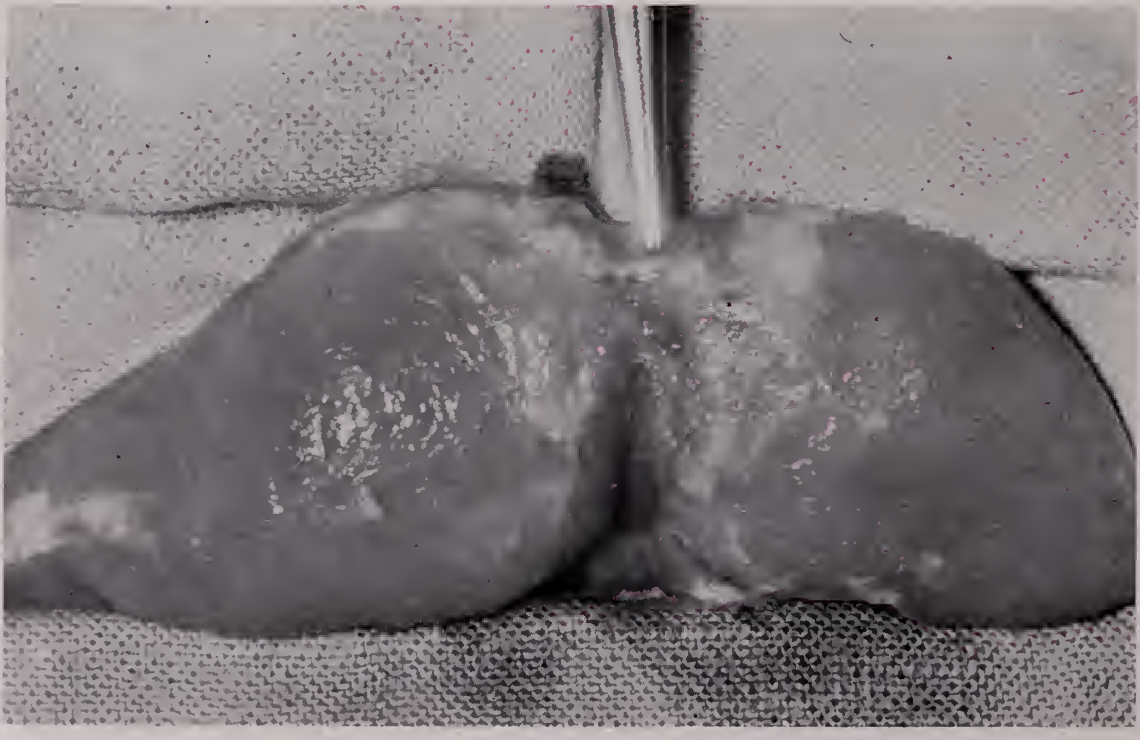

Fig. 2. Operative photograph showing the site of perforation.

SINCE 1805 WHEN Baillie[1] first described primary or nonspecific ulcers of the small bowel, occasional papers on the subject have appeared, but without a significant contribution as to probable etiology. Zollinger and Ellison reported the relationship of jejunal ulceration to islet cell tumors of the pancreas in 1955,[2] and no doubt a few of the cases previously reported as nonspecific ulcer of the small bowel fall into this category. Currently there are about 180 cases of nonspecific ulcer of the small bowel found on review of the literature.[1-23] The most recent report by Baker et al. documents an apparent increase in the incidence of the lesion as well as a possible correlation of it with oral enteric-coated potassium therapy.[23] Further support for these views was found in the five cases reported here, four of which had been on oral enteric-coated potassium therapy prior to surgical confirmation of the lesion, and all of which occurred in 1963 and 1964, the last two years of a ten-year review of the pathology records of three Minneapolis hospitals. All of the cases are consistent with the classification of nonspecific small bowel ulcer.

Pathologic Findings

Pathologically the lesion is a well-defined ulcer with underlying acute or chronic inflammatory reaction similar to peptic ulcer of the stomach. The more chronic cases show varying amounts of submucosal fibrosis and stricture. The adjacent bowel is normal, and mesenteric vascular and lymphoid change is significantly absent.

Symptoms

Symptoms are those of ulcer complication, i.e., partial intestinal obstruction, perforation, or hemorrhage. Pain is described as gnawing or cramping, and the site is most commonly periumbilical or just below and to the left of the umbilicus. Intermittent "bloating" is generally associated with loss of appetite, nausea, or vomiting.

Diagnosis

The diagnosis is rarely possible preoperatively, but it should be seriously entertained in cases of small bowel obstruction in the absence of hernia, previous abdominal surgery, and history consistent with gallbladder disease. Oral potassium therapy is an added clue that cannot be overlooked. Flat and upright X rays of the abdomen are of value in confirming intestinal obstruction or hollow viscus perforation. A barium study in those with vague or intermittent symptoms may confirm the presence of a distended loop proximal to the lesion, and occasionally a filling defect has been reported. Rarely is massive intestinal hemorrhage a finding, but anemia[5,7,21] and melena may occur. Guaiac positive stool was the most common positive laboratory finding in the report of Goehrs.[13]

Report of Cases

Case 1

This 63-year-old white female was admitted to the hospital January 2, 1962, with recurrent abdominal cramping, nausea and vomiting. Symptoms had been vague, transient, and recurrent over a three-year period. On preoperative study a single gallstone in a functionless gallbladder was found; and on one flat and upright X-ray examination there was a suggestion of partial small bowel obstruction. General physical examination was within normal limits, and the patient was on no medications.

At laparotomy January 3, 1962, a firm stenotic lesion of the small bowel 18 inches proximal to the ileocecal valve was found. The bowel distal to this point was reduced in calibre, but there was no significant proximal dilatation. The mesentery was normal. Further exploration was normal except for a diseased gallbladder containing a single ovoid 12x11x11 mm. cholesterol stone. Segmental resection and end-to-end anastomosis of the bowel along with cholecystectomy and incidental appendectomy was done. Recovery was uneventful.

Pathologically the lesion showed mucosal ulceration, submucosal acute and chronic inflammatory cells and fibrosis, consistent with nonspecific ulceration of the small bowel.

Case 2

A 29-year-old housewife was admitted to the hospital April 3, 1964, with cramping lower abdominal pain, abdominal distension, lower abdominal tenderness, hyperactive bowel sounds with intermittent rushes and rectal tenderness on the left. Flat and upright films of the abdomen revealed findings consistent with small bowel obstruction. Symptoms subsided overnight and she was discharged.

Additional history revealed that in January, 1964, she had been taking, for severe headaches, an oral enteric-coated diuretic with potassium, resulting in symptomatic improvement in the frequency of her headaches. Ten days before her admission, cramping abdominal pain began.

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*Read before the Minneapolis Surgical Society.

She was readmitted April 13, 1964, with identical symptoms which did not subside. Therefore, on April 15, 1964, laparotomy was carried out.

At surgery a 5-mm. area of stenosis was found in the ileum three feet proximal to the ileocecal valve. The bowel distal to the lesion was collapsed; proximal to the lesion it was dilated and edematous. A 9-cm. segment of small bowel was resected and an end-to-end anastomosis done. Recovery was uneventful and the patient has remained well to date.

The resected specimen showed mucosal ulceration and an acute submucosal inflammatory infiltrate at the site of the lesion (Fig. 1). The lesion was consistent with the diagnosis of nonspecific ulcer of the small bowel.

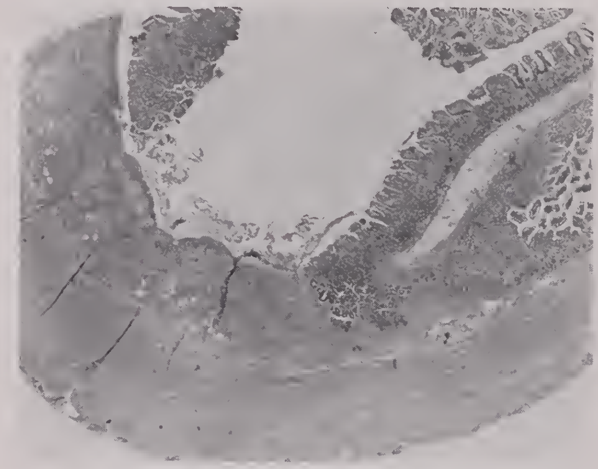

Fig. 1. Case 2. A section showing the mucosal ulcer, and submucosal acute infiltrate and edema.

Case 3

A 24-year-old housewife was admitted to the hospital with complaints of marked bloating and persistent generalized abdominal pain which had had sudden onset after the evening meal the previous day.

Examination revealed abdominal distension, minimal lower abdominal guarding and rebound tenderness. The temperature was 100.2. White blood count was 20,000 with 92% polymorphonuclear cells. As culdoscopy was being done, an abundant amount of thin, greenish-white, odorless fluid was released. Flat and upright films of the abdomen showed free air under both leaves of the diaphragm.

Past history revealed a sixty-five-pound weight gain in a post-partum period one year before the present illness, and in an effort to reduce weight an oral diuretic with potassium was taken in November, 1963. In February 1964, the patient went on a self-prescribed grapefruit and eggs diet. Two days later she developed severe bloating, abdominal pain, and nausea. Symptoms subsided with resumption of a normal diet and discontinuation of the diuretic. She claimed she never resumed the diet or took any diuretic in the 60-day interval from that time to the onset of the present illness.

Laparotomy April 24, 1964, revealed a perforation at the site of a circumferential narrowing in the lower jejunum (Fig. 2). The greenish-milky fluid aspirated at culdoscopy was present over the loops of bowel in the lower half of the abdomen and in the pelvis. There was also some distension of the small bowel proximal to the lesion; otherwise, the small bowel and mesentery were normal. A 12-cm. segment of small bowel was resected and an end-to-end anastomosis done. Recovery was uneventful.

Examination of the specimen revealed a circumferential mucosal ulceration with a small perforation on the antimesenteric border. Microscopically, the lesion was an acute ulcer with an acute inflammatory infiltrate limited to the wall at the site of perforation (Fig. 3).

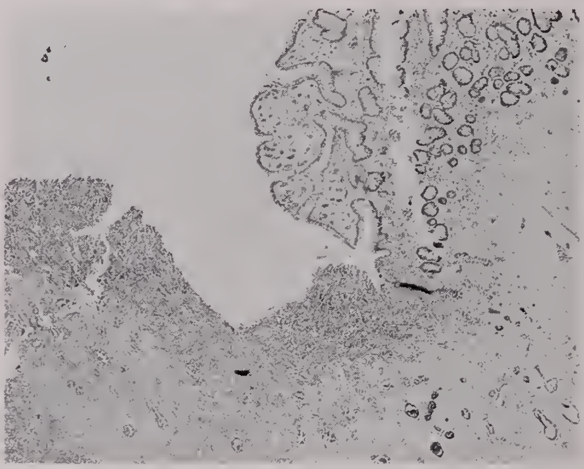

Fig. 3. Case 3. Section showing the acute ulcer with perforation and adjacent normal small bowel.

Case 4

A 59-year-old male was admitted to the hospital May 3, 1964, with cramping abdominal pain of two days' duration. Two weeks prior to admission he had had an episode of weakness, faintness and transient numbness of the right leg, with a similar episode the following day. On examination there was no neurological deficit. These episodes were thought to represent mild cerebrovascular accidents. An enteric-coated diuretic containing potassium was prescribed. For two days after the medication was started the patient complained of mild abdominal cramping, but was asymptomatic during the remaining ten-day interval before the onset of the present illness. Examination revealed a blood pressure of 140/90. The abdomen was distended and there was tenderness to the left of the umbilicus. Bowel sounds were slightly hyperactive. White blood count was 11,900 with 90% polymorphonuclear cells. Flat and upright films of the abdomen were consistent with a partial small-bowel obstruction. Symptoms subsided with rest and intravenous fluid therapy, and the patient was discharged. Symptoms recurred after discharge with almost daily mild abdominal cramping, and on May 25, 1964, he was readmitted with recurrent small bowel obstruction. The diuretic with potassium was taken during the interval between hospital admissions.

At laparotomy May 25, 1964, a 5-mm.-long stenosis of the ileojejunal area of the small bowel was resected and an end-to-end anastomosis was done. Recovery was uneventful, and the patient has remained well to date.

Sections of the lesion revealed a circumferential mucosal ulceration with both acute and chronic infiltrate at the ulcer base. Submucosal edema and fibrosis were noted. The lesion was considered consistent with a nonspecific ulcer of the small bowel.

Case 5

A 46-year-old male was admitted to the hospital November 7, 1963, with constant right lower abdominal pain and frequent loose stools of one month's duration. One year previously the patient had undergone an extensive hospital evaluation for episodes of dizziness, weakness, palpitation, and sweats involving the head and neck, thought possibly to be due to pheochromocytoma. Tests failed to confirm this impression, however. Because of hypertension (180/110) an enteric-coated diuretic containing potassium was prescribed in December 1962. The patient developed right lower quadrant pain in March 1963, occurring two to three times a week and lasting from a few minutes to one and one-half hours. He was hospitalized May 2, 1963, because of the abdominal pain. Studies were negative except for the admission flat and upright films of the abdomen which showed small bubbles of gas scattered throughout the small bowel. The diuretic was continued after discharge from the hospital.

Laparotomy was done November 8, 1963. A stenotic lesion in the ileum 18 inches proximal to the ileocecal valve was resected and end-to-end anastamosis was done.

There was a 1-cm. circumferential mucosal ulcer at the site of the lesion. Sections showed an acute inflammatory base, and also submucosal edema and fibrosis.

Following discharge from the hospital this patient resumed therapy with the enteric-coated diuretic with potassium until July 1964, without further abdominal complaints.

Discussion

With the advent of an apparent increase in incidence of nonspecific small bowel ulceration and a suggestive correlation with the ingestion of a chemical agent in a high percentage of the recently reported cases, further detailed documentation of similar cases is essential. Four of the five reported cases in this series were taking or had been taking an enteric-coated oral diuretic containing 500 mgm. of potassium chloride prior to the onset of symptoms. Three different preparations were represented. All five cases occurred one to three years after the introduction in this area of enteric-coated diuretic preparations containing potassium chloride, whereas none were found in the pathology records of the three hospitals in the prior eight years of a ten-year review.

Duration of therapy prior to the onset of symptoms varied from a few days to three months. In one case acute symptoms developed while on potassium therapy and subsided after cessation of medication, only to recur two months later.

Duration of symptoms varied from one to nine months before a surgical diagnosis was made. Significantly, three of the patients were healthy individuals with no cardiovascular disease. Two were young housewives in their twenties. The earlier literature on nonspecific small bowel ulceration showed a predominance of perforated ulcers (81% of 130 cases reviewed by Evert in 1948).[6] Cases reported after 1960 appear predominantly as partial intestinal obstructions; stenosis is the prominent feature at surgery. Nineteen of the last twenty-three cases presented with symptoms of intestinal obstruction. The other four with perforations gave histories suggestive of pre-existing partial obstruction and had some degree of stenosis noted at the site of perforation. With this possible exception the lesions occurred predominantly in the lower jejunum or ileum and were pathologically similar to those previously reported. Surgical management was indicated in those with complications of the ulcer; morbidity and mortality were low.

Conclusion

Although there is suggestive evidence that oral therapy with enteric-coated potassium medications may be a contributing etiological factor, one case in this series and all of the cases prior to the introduction of this form of therapy must be explained on some other basis.

Acknowledgment

The authors are indebted to Dr. B. D. Mitchell and Dr. D. J. Moos for the privilege of reporting cases 5 and 4.

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WHAT'S YOUR DIAGNOSIS?

A fifty-year-old, previously well railroad conductor noted the onset of mild "burning" distress across the mid-abdomen a week prior to admission. Three days prior to admission he developed intermittent crampy pains in the left upper abdomen. There was no nausea, vomiting or loss of appetite. His bowels continued to move with a normal-appearing stool. His past history was negative except for rheumatic fever at age thirteen and a hemorrhoidectomy a year previous to admission.

Physical examination was negative except for left upper abdominal tenderness without distention, rigidity, or rebound. There was mild left costovertebral angle tenderness.

Laboratory studies showed a hemoglobin of 14 gm %, a WBC of 7,000 with a differential of 57% pmn's and 39% lymphocytes. The sedimentation rate was 9 mm. in one hour. The urinalysis was normal. Serum amylase was normal. X-rays of the chest and abdomen were normal. The ECG was normal. Upper GI x-rays with small bowel follow-up were normal. On the third hospital day the diagnosis became evident.

What is your diagnosis? Turn to page 918.

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Side Effects: Side effects are relatively uncommon but among those reported are gastrointestinal irritation, sedation, dizziness, cutaneous manifestations, restlessness and insomnia.

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6 to 12 months–4 mg. (½ tsp. q.i.d.)
1 to 2 years–5 mg. (½ tsp. 5 times daily)
2 to 5 years–6 mg. (1 tsp. t.i.d.)
5 to 8 years–8 mg. (1 tsp. q.i.d.)
8 to 12 years–10 mg. (1 tsp. 5 times daily)

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Editorials

Small Bowel Ulcers

A SCIENTIFIC presentation in this issue of Minnesota Medicine* presents five patients recently operated upon for stenosing ulcers of the small intestine. The authors call attention to the possible relationship of these ulcers to therapy with oral enteric-coated potassium chloride medications.

During recent months several pharmaceutical companies have produced medications combining hydrochlorothiazide and potassium chloride in a common enteric-coated tablet. This type of combined therapy was implicated as a causative factor in small bowel obstruction in November 1964, in a scientific article in the Journal of the American Medical Association by Baker, Schrader, and Hitchcock. These authors presented 12 patients with nonspecific ulceration and stenosis of the small intestine, 11 of whom had received medication with the combined hydrochlorothiazide and potassium chloride tablets. The 11 cases in the November report occurred over a period of 15 months, and statistical analysis indicated that patients on potassium-containing, enteric-coated medications have a significantly higher risk for development of an ulcerating and obstructing small bowel lesion than other patients receiving potassium chloride medication without the enteric coating.

The clinical study presented in this issue of the journal adds to the evidence that enteric-coated potassium chloride is a potentially dangerous form of potassium therapy. When the potassium salts are suddenly released to the mucosa in high concentration at a specific pH of the intestinal content, cellular damage leads to ulceration and fibrosis. Evidence garnered from several parts of the world now indicate this to be a problem wherever this form of potassium therapy is used.

Physicians at the Hennepin County General Hospital are now encouraged to prescribe hydrochlorothiazide as a single preparation, and to provide supplemental potassium as a separate medication dissolved in orange juice or some other fruit juice. At this time all evidence indicates that hydrochlorothiazide alone does not cause intestinal ulceration and stenosing with subsequent obstruction. Also, present evidence indicates that potassium chloride dissolved in a liquid does not harm the intestine. Practicing physicians are alerted to the possible dangers inherent in the combined form of therapy.

Claude R. Hitchcock, M.D.
Minneapolis, Minnesota

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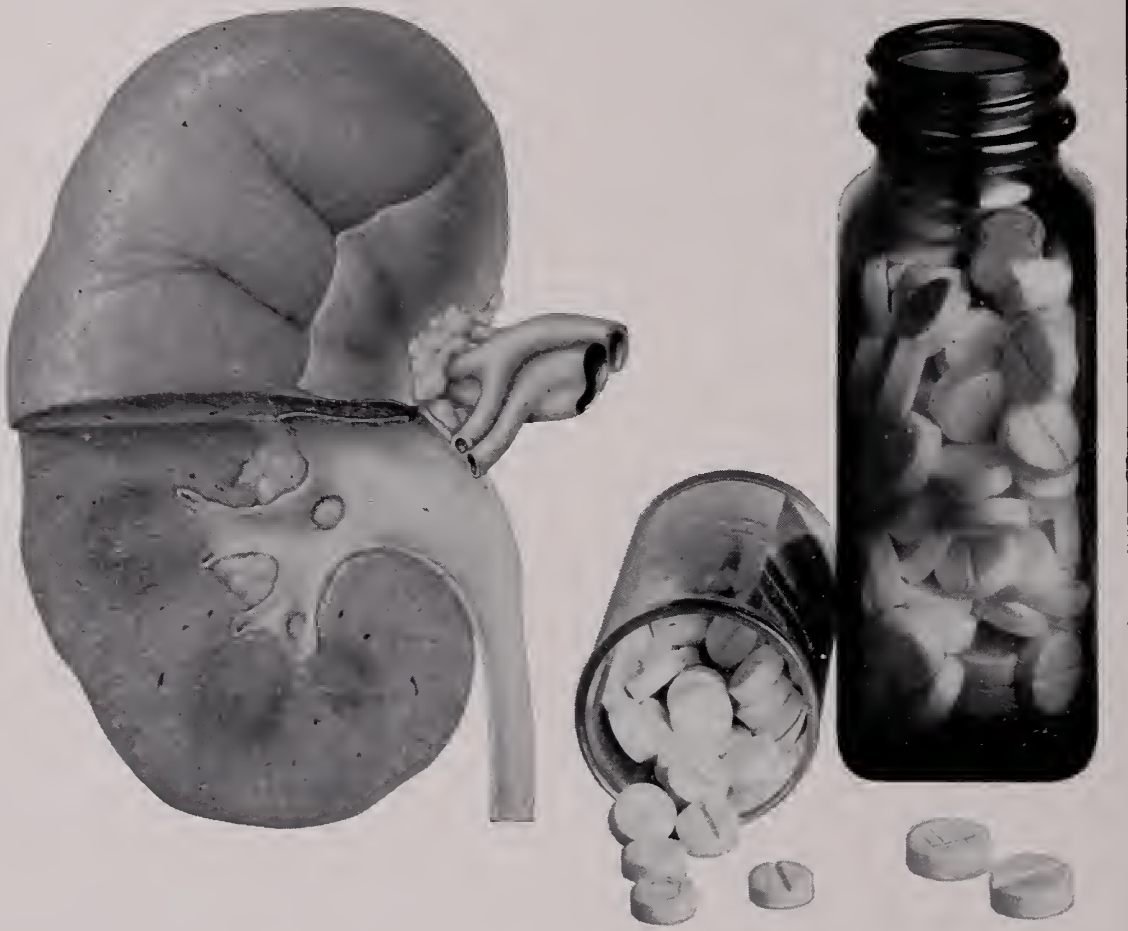
*See Page 880.

at Merck Sharp & Dohme...



understanding... precedes development

The development of chlorothiazide and probenecid were events of major importance, but perhaps even more important for the future was the Renal Research Program by which they were developed. When Merck Sharp & Dohme organized this program in 1943, it was expressing in action some of its basic beliefs about research:

- Many problems connected with renal structure and function were still undefined or unsolved. The Renal Research Program would begin its basic research in some of these problem areas.
- From knowledge thus acquired might come clues to the development of new therapeutic agents of significant value to the physician.

For example, the Renal Research Program put fifteen years into this search before chlorothiazide became available. But because these years had first led to a greater understanding of basic problems, the desired criteria for chlorothiazide existed before the drug was developed.

Along with other research teams at Merck Sharp & Dohme, the Renal Research Program continues to add new understanding of basic problems—understanding which will lead to important new therapeutic agents.

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Blood Transfusion and the Clinician

Within the past two decades the technique of blood transfusion has been developed to a point where it is regarded by many as a routine procedure, and the ever threatening dangers are sometimes not fully appreciated. Elsewhere in this journal* Dr. Huestis emphasizes some of the problems and pitfalls with which the laboratory of a blood bank has to deal on a daily basis.

Incompatibility of blood types, however, is only one of the dangers accompanying blood transfusion. The danger of homologous serum hepatitis not only exists, but at the present time can be neither completely prevented nor controlled. Other consequences, such as overloading of the recipient's circulation, do not concern the blood bank directly and are the responsibility of the clinician.

The overwhelming majority of hemolytic reactions due to the transfusion of incompatible blood are not the result of laboratory errors but fall in the category of "clerical error."

Within the blood-bank laboratory they can be avoided if the bookkeeping system is as simple as it is rigidly controlled. Human errors will increase in direct proportion to multiple transcriptions of data. The less copying and transcription the less error! Most blood banks have recognized this problem and eliminated or minimized its dangers. However, a well organized and operated blood bank will be powerless to prevent a tragically high incidence of transfusion reactions if it has to operate within a clinical organization which permits laxity and carelessness on wards and in operating rooms, because most "clerical errors" occur outside the blood bank proper. The most common errors arise in the following situations:

1. Obtaining the recipient's blood sample, the "pilot tube." All efforts should be made to have blood-bank personnel obtain the patient's blood sample rather than physicians or general laboratory personnel. If circumstances necessitate the drawing of a pilot sample by persons other than blood-bank personnel the patient's full name, hospital number, the date and initials of the individual who obtained the "pilot" sample, must be written in ink on a label, which is firmly affixed to the glass tube, not merely rolled or folded around it.

2. Only blood-bank personnel may issue blood. Access to blood-bank refrigerators must be strictly forbidden to anyone else.

3. If several blood units were issued for a patient and temporarily stored in a ward refrigerator, we would create a situation which facilitates the confusion of blood units intended for different patients. Therefore, only one unit should be issued for any one patient at a time for ward use, even though successive transfusions are planned. In the case of surgery all units which have not been used during operation, will be returned to the blood bank immediately after termination of surgery. The loss of time spent in repeated trips of ward attendants to the blood bank, will be rewarded by a decrease of transfusion catastrophes.

4. Improper identification of the recipient has been the most important clerical error. The recipient will be identified not only by full name but also by hospital number, and these data will have to be identified on the patient's identification bracelet (or bed tag), the label on the blood unit and the request sheet. The transfusion may be undertaken only if all data agree.

Other precautions will be followed as a matter of routine. The sample of a patient's blood "pilot tube" may be used for cross-matching only for a period of 3-5 days. A fresh "pilot" will have to be employed for any transfusion thereafter. After termination of each transfusion the empty bottle or plastic bag must be returned to the blood bank, where it will be kept for 48 hours. Late transfusion reactions, particularly those in which bacterial contamination of the donor blood is suspected, may then be investigated

Continued

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*See Page 857.

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Whenever a transfusion reaction is suspected the following steps should be taken:

1. If a hemolytic reaction is suspected (tingling sensation, pain in chest and back, fever, chill, tachycardia, tachypnea, hypotension, etc.) the transfusion is to be stopped immediately. Hydrocortisone may be administered intravenously in an attempt to minimize the hemolytic reaction. Twenty-five grams of mannitol may be infused intravenously in order to promote diuresis and dilution of hemoglobin in the renal tubules. The administration of mannitol may be repeated if successful.

2. The blood bank is to be notified immediately.

3. A sample of the patient's blood will be collected in a tube which contains an appropriate anticoagulant. Although these tubes are available commercially as rubber-stoppered vacuum tubes, artificial hemolysis should be avoided by releasing the vacuum and transferring the blood gently from the syringe, avoiding turbulence or the formation of air bubbles. The plasma of this specimen will then be used for the quantitative determination of free plasma hemoglobin. This will be repeated after 4 and 12 hours.

4. Another blood sample will be used for the determination of serum bilirubin and blood urea nitrogen. This will be repeated after 12 and 24 hours.

5. Blood cultures will be obtained and the material incubated at 37 C and 4 C under aerobe and anaerobic conditions.

6. The patient's urine will be collected on a 24-hour basis for determination of urine hemoglobin as well as the quantity of urine output.

7. The blood unit which was involved in the suspected transfusion reaction will be returned to the blood bank for verification of the crossmatch as well as for bacterial culture at 37 C and 4 C under aerobe and anaerobic conditions. Bacteremia due to contamination by donor blood can be assumed only if the same organism is cultured from the donor bottle as well as from the recipient's blood.

Although the danger of serious transfusion reactions can be minimized by the combined efforts of laboratory and the clinical services, a rare human error cannot be eliminated completely. Whenever such an accident occurs the responsibility will be easier to shoulder if the transfusion was "necessary," i.e., if it was administered for the type of blood loss or anemia which could not have been remedied satisfactorily in any other way.

Horace H. Zinneman, M.D.
Minneapolis, Minnesota

Peritonitis and Gas Gangrene

Although many advances in the diagnosis and treatment of various types of infections have been made in the past two decades, infections within the peritoneal cavity are difficult to study bacteriologically and therefore difficult to treat effectively. If the abdominal cavity is surgically explored and if adequate fluid or tissue is obtained for culture, the etiologic agent usually can be identified within a few hours or a few days. However, surgical exploration is not always advisable and, even after laparotomy, a period of time often passes before cultural data are available. During this interval the cause and, therefore, the correct management of the infection are not apparent. To date there is no single antibiotic agent or any combination of agents that is effective against all of the various strains of bacteria that may cause peritonitis. For these reasons, continuing study of the bacteriologic and pathologic aspects of peritoneal infections is imperative.

The spectrum of organisms that may produce peritonitis is wide, and the infection may range from a very acute, rapidly lethal process to a low-grade indolent infection. In most instances, the infections are due to a mixture of organisms. The flora of the intestinal tract participate in many of these.

Continued

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Enteric bacilli are frequently present, but in many instances, Bacteroides and various strains of Clostridium and enterococcus are considered more important in the pathogenesis. Some of these organisms are capable of producing gas in the tissues. E. coli and certain species of Clostridium may be responsible for considerable amounts of gas. The detection of gas in infected tissues, therefore, is not necessarily a sign of gas gangrene due to Clostridium organisms since E. coli and other organisms are capable of producing gas. Of course, the possibility of gas gangrene due to species of Clostridium always must be considered seriously, since disregard for this type of infection would be disastrous.

When Clostridium organisms are cultured from the human body, the question frequently arises as to whether antitoxin should be given. Gas gangrene is a virulent and frequently fatal disease. All measures that might affect the outcome favorably must be employed. However, gas gangrene antitoxin is derived from horse serum, and its use may be accompanied by any of the hypersensitivity reactions so often associated with the administration of horse serum to man. Clostridium organisms are normal inhabitants of the intestinal tract and at times can be cultured from tissues in which there is no evidence of gas gangrene and in which this infection does not develop. Careful physical examination and experienced clinical judgment are necessary in the determination of the type of treatment that should be given when the "gas gangrene" strains of Clostridium are cultured from tissues.

Blood cultures should be obtained from all patients with peritonitis. If tissue or fluid from the peritoneum cannot be obtained for culture, blood cultures often provide essential bacteriologic information regarding the etiologic organism or organisms. Furthermore, if bacteremia is present, the possibility of impending or associated bacteremic shock must be considered, and the patient must be managed accordingly.

In recent years, the use of hyperbaric oxygen in the treatment of infection due to anaerobic or microaerophylic organisms such as species of Clostridium has been studied in a small number of infections. Encouraging results in the treatment of gas gangrene infections have been reported. Unfortunately, the use of hyperbaric oxygen is associated with certain hazards. Therefore its widespread use in the treatment of infections must await further study by experienced investigators.

Donald R. Nichols, M.D.*
Rochester, Minnesota

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*Section of Medicine, Mayo Clinic and Mayo Graduate School of Medicine.

Reference

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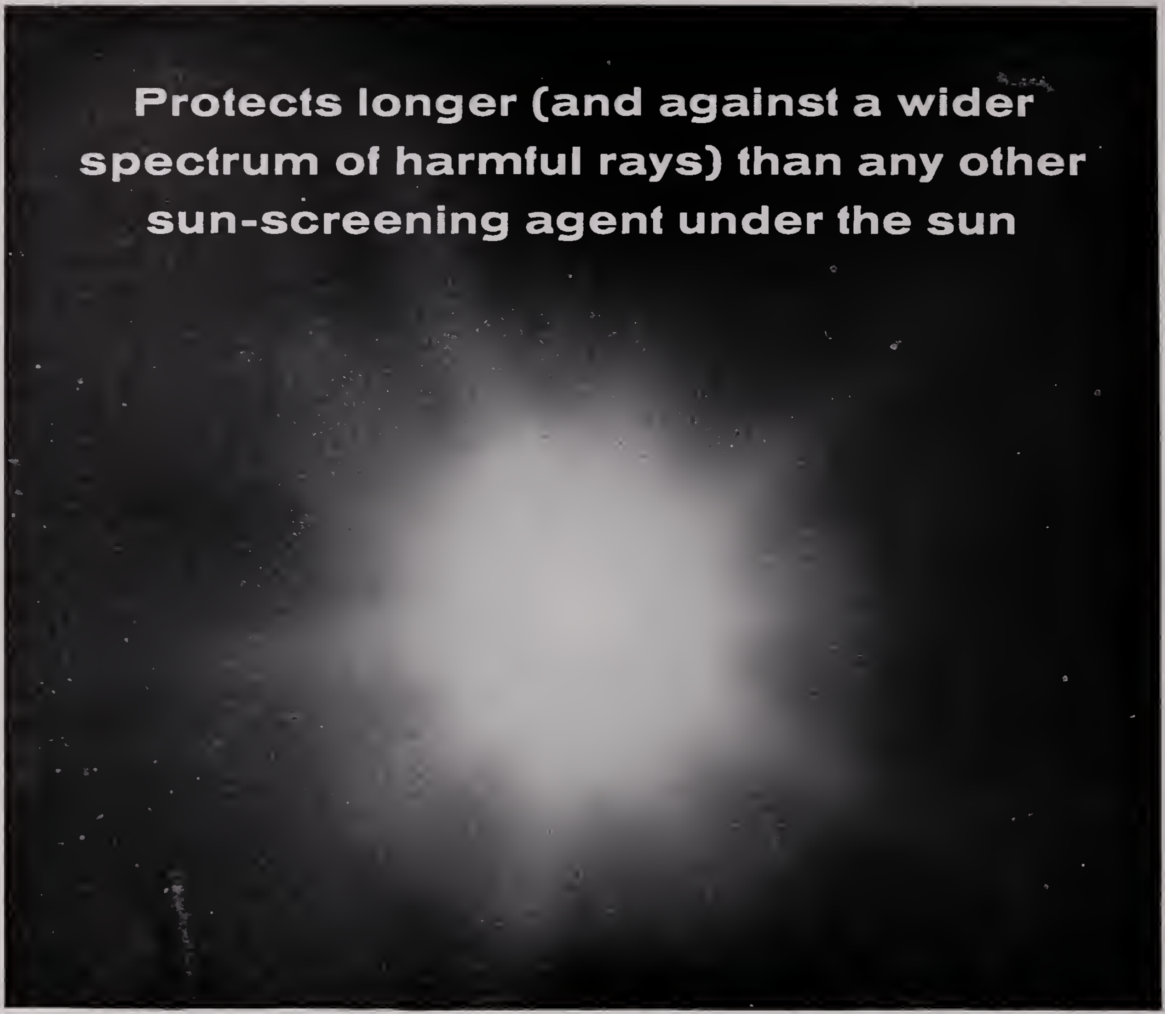
Letter to the Editor:

To the Editor: Having noted your comment in the April issue of Minnesota Medicine on the "almost unlimited potential resources of the sea to provide for Earth's exploding population," I would like to counter by asking: Granted that the ocean could provide adequate food for our over-spawned masses, *who wants to eat standing up!* — E.R.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Precancerous Dermatoses

CANCER EDUCATION campaigns being carried out in this country are increasing the number of patients consulting physicians for various tumors or tumor-like lesions arising on the skin. With aging, the number and variety of such tumors increase. Fortunately the overwhelming majority of skin tumors are benign. Most of them are so characteristic as to enable the physician to make an accurate diagnosis on inspection alone. In others histopathologic examination is needed. The sooner an opinion can be given the greater the opportunity of curing the lesion if it is actually malignant.

The premalignant or precancerous lesions, discussed in the June issue of MINNESOTA MEDICINE* as a broad group are often seen and usually easily recognized. The most common and important lesion in this group is the actinic or senile keratosis. Recent inroads have been made regarding the etiologic factors playing a role in the premalignant lesions of the skin. A variety of biological, physical, and chemical factors have been studied experimentally in animals and have provided substantial support for the opinion that these factors are also operative in human skin cancers. The so-called biological factors are: inherited susceptibility, skin color, sex, specific sites and age. The important physical factors are mechanical trauma, burns, actinic radiation or ultraviolet light, ionizing radiation from X-ray sources, radium radioisotopes, and cosmic rays. Among the chemical factors which have been shown to cause precancerous and cancerous lesions of human skin are materials contained in or derived from petroleum, coal, shale and compounds of arsenic.

Probably the most important etiologic factor today is sunlight. This is exemplified in many studies showing the low rate of skin cancer in the negro as compared to the white population. Significantly, cutaneous cancer is much more common in the southern than in the northern latitudes. An examination of cancer rates for all organs reveals that only in the case of skin cancer is there a clear-cut difference on the basis of geographic location, the rate being greater in the south than in the north. A recent survey in Honolulu demonstrates that skin cancer is 45 times as common among Caucasians as among non-Caucasians and over 90 per cent of skin cancers are found on the exposed areas such as the face, neck, hands and forearms. Further evidence of the etiologic importance of solar radiation is demonstrated in outdoor workers who have a much higher incidence of skin cancer than those working indoors. It has also been shown that ultraviolet radiation induces cancer of the skin in mice and rats.

Prevention of precancerous and cancerous lesions means essentially the avoidance or removal of those factors which may influence the development of these lesions. It may be advisable to acquaint young individuals who have outdoor occupations with the consequences of long-term sunlight exposure. This is particularly important for individuals with blue eyes and fair complexions. An effective sunscreen preparation such as 15% para-aminobenzoic-acid ointment, which screens out rays in the range of 2800 to 3100 Angstroms can be prescribed when sun exposure is unavoidable. When early changes are visible, recreational sun exposure and the use of photosensitizing drugs or substances should be curtailed. Patients showing these precancerous lesions should be advised to have periodic medical examinations. Any lesion showing suspicious changes should be biopsied as should all new lesions suspected of being potentially malignant. The prevention of cutaneous carcinomas is practical only insofar as we can recognize and eradicate such etiologic factors as chronic sunlight exposure, intermittent trauma and chemical carcinogens and adequately prevent, treat or keep under surveillance the various premalignant conditions.

Alvin S. Zelickson, M.D.
Minneapolis, Minnesota

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*Minnesota Med 48:742, 1965.

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Laboratory Standards in Minnesota Hospitals

THAT "TROUBLE IS NORMAL," is a Dr. Gerald Evans' axiom which is firmly drilled into the skulls of clinical pathology residents, those peculiar animals usually found roaming semiconsciously through that forest of threatening machines, graphs, complex glassware, chemicals, slide rules, variously assorted body "specimens," ringing telephones, coffee, and gorgeous girls, the conglomerate of which is called a clinical laboratory. As a matter of fact, one might say that the excellency of a clinical laboratory is directly proportional to its ability to discover and correct its errors.

In this issue of Minnesota Medicine* is a report of a two-year study of clinical chemistry determinations in Minnesota hospitals conducted by the Minnesota State Department of Health. This study was more than a mere survey of laboratory performance, however. It is one thing to show a laboratory that it has erred and quite another to correct the errors. As was true of many other past surveys, the present survey did indeed show that clinical laboratories are having troubles. But the intent of the present study was much greater than just to point out laboratory difficulties. Its major purpose was to see whether a series of performance surveys interspersed with technical consultations could improve the quality of hospital laboratory performance in clinical chemistry.

One hundred and ten hospitals voluntarily participated in the study. Over two hundred hospitals were invited to participate. The larger the hospital-bed capacity, the greater was the percentage of participation. For example, 94.1% of the invited hospitals with over 250-beds took part; whereas only 32.6% of the hospitals invited under 25-beds participated. The same relationship held true of those completing the study. One hundred per cent of the over 250-bed hospitals group completed the study, whereas only 62.5% of the under 25-bed hospitals group completed the study.

Eighteen separate surveys were conducted over a period of 22 months. The surveys were divided into three phases. Phase I, a preconsultation phase, was used to establish a base line of performance and divide the laboratories into three groups. The best performing one third of the hospital laboratories was called the criterion group. This group received no other help except that they were notified of the results of one survey before the next survey specimens were mailed. The remaining two thirds were divided randomly into a control group and a consultation group. The control group represented a group whose results were similar to the consultation group in Phase I but whose improvement (if any) in Phases II and III would be from self help only. Each hospital in the consultation group received at least three visits from a consultant clinical chemist during Phase II. Chemistry workshops attended by at least one member from each consultation group hospital were also held. Phase III was a post-consultation survey. The survey specimens to be determined were glucose, calcium, chloride, hemoglobin, urea nitrogen, total protein, uric acid, and cholesterol. The hospitals needed to do only those tests which were routinely done in their labs. The labs also completed questionnaires regarding the level of training of their personnel, administration, type of equipment, supplies, etc.

The results of the study are not too surprising. The best performing labs were those which had the best trained personnel and supervision, i.e., the greatest number of American Society of Clinical Pathology registered technologists (or equivalent), and supervision by pathologists. In general, these were also the hospitals with the largest bed capacities and the heaviest work loads. Furthermore, the best performing labs in Phase I also showed the greatest improvement in Phases II and III. Well-trained personnel were able to improve through participation in evaluation studies alone. This was not true for less well trained personnel who did not improve by mere participation in an evaluation study.

As far as consultation is concerned, a clear-cut effect was noted only in one determination. There was a significant improvement in

Continued

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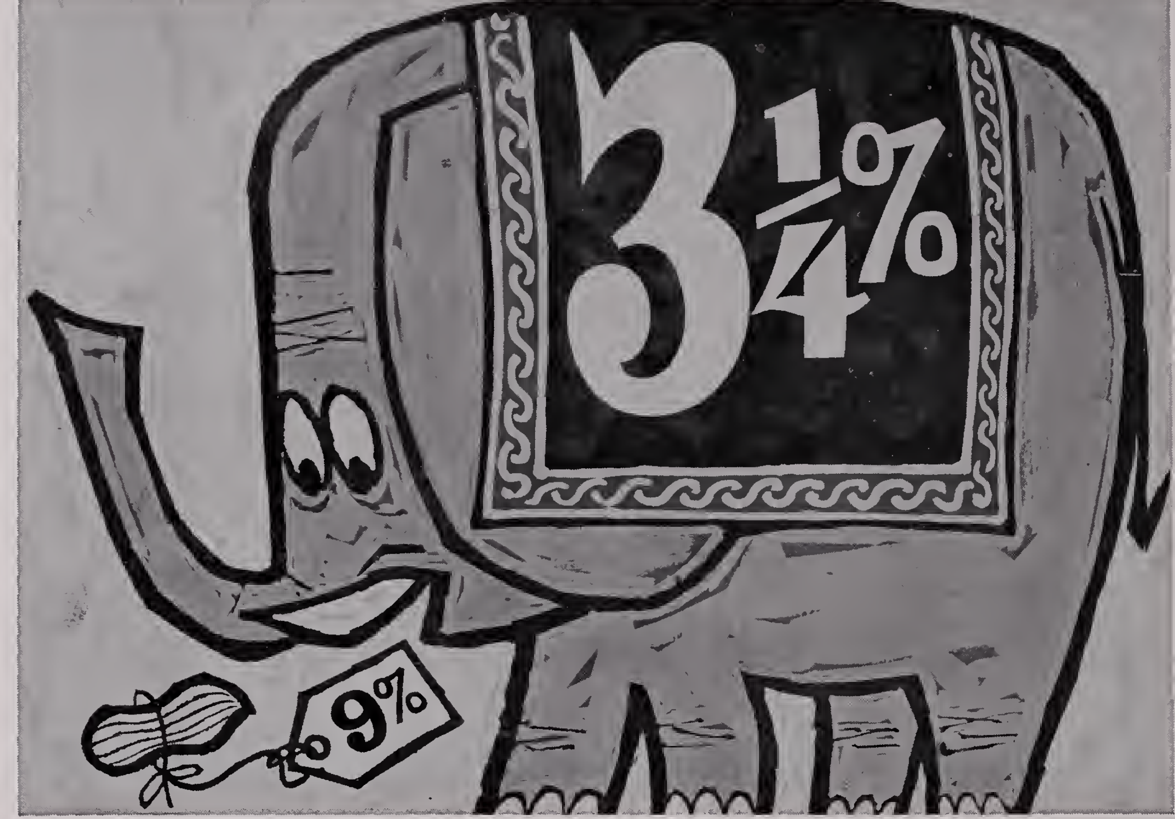
*See Page 939.

Riddle:
When is 3¼% larger than 9%?



Answer! When it represents *keepable* income from tax-free municipal bonds! A 9% yield from ordinary stocks may seem like a nice profit. But, it's really small peanuts, if you're in a high income bracket. Reason? Federal and state income taxes can take a huge amount of that profit away. Not so with *tax-free* municipal bonds! They allow you more "keepable" income . . . more big peanuts to salt away in your trunk! First National Bank offers a large selection of these bonds. Sound good? Then mail the coupon below for our free booklet "The Story Behind Municipal Bonds," as well as our handy "Tax Exempt Versus Taxable Income Table." Both give you vital information that can save you money. Or call our Investment Department (221-9463). So make like an elephant—don't forget—tax-free bonds can give you more *keepable* income!

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hemoglobin determination in the consultation group in both accuracy and precision, and the control group did not show this improvement. The only other significant net change was for the serum calcium determination which actually showed a deterioration in accuracy.

The need for better trained personnel and constant supervision by qualified physicians, especially in "smaller" hospital laboratories, is evident. Occasional consultations will not suffice. The stimulus for improvement in laboratory performance should come from the practising physicians. That some physicians are lax in demands on their labs is evident from the number still using total reducing substance methods for reporting blood sugars instead of true glucose methods. It behooves all clinicians to study the article by Merritt, et al. in this issue of Minnesota Medicine.

The ideal hospital laboratory would have adequate numbers of well-trained ASCP technologists; American Board certified clinical pathologists; daily quality control programs to determine reproducibility of results; outside standards, surveys and check specimens to determine accuracy; calibration of laboratory equipment such as photometers, cuvettes, and quantitative glassware; and finally, approval of the laboratory by the American College of Pathologists inspection program. Even under these theoretically ideal conditions errors are still frequent. These are individual errors which are difficult to control and are of great variety. Clerical recording errors, transposition of colorimeter readings, misplaced decimal points, unnoticed scratched cuvettes, unnoticed chipped pipette tips, stasis of blood in drawing, drawing while I. V. running, physiologic stress phenomena not taken into consideration, using the wrong pipette, and medications that interfere with methodology or prejudice the results are only a few examples of such errors. The laboratory depends upon the astute practising physician to help control these individual errors. Clinical lack of correlation with laboratory results should be reported to the lab immediately. A happy, relaxed, laboratory atmosphere with good morale is also important in keeping individual errors at a minimum. The physician can do much for laboratory morale and actually improve the laboratory services given to him, by not abusing "stat" and "emergency" lab requests and by vocalizing his lab criticisms directly to those in charge of the laboratory in a constructive and friendly manner. "To err is human; to forgive divine."

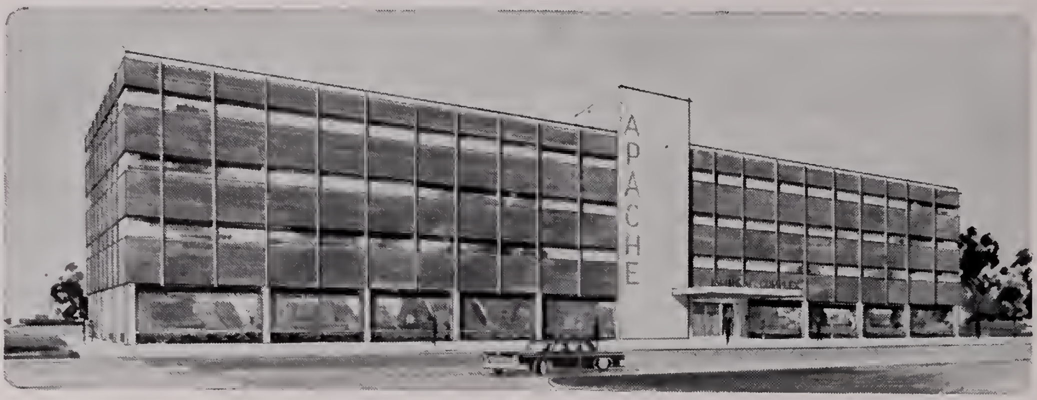
Martin A. Segal, M.D.
Methodist Hospital
St. Louis Park, Minnesota

Community Service Conference on Neurological Disorders

The University of Minnesota Medical Center under the Comprehensive Clinic Program, is now engaged in a project designed to enhance service to patients with neurologic disease through greater community-university cooperative participation. As a part of this program, weekly or bi-weekly conferences are held at the University in which the referring physician participates along with the neurologist, psychologist, and other consultative community and university personnel who have seen the patient. Publication of selected conferences are published in "Minnesota Medicine" as a part of this project.

Inasmuch as women are always willing and able to explain their strong points, they leave us to guess at their weak ones. — Balzac

We all have weaknesses. But I have figured that others have put up with mine so tolerably that I would be much less than fair not to make a reasonable discount for theirs. — William Allen White



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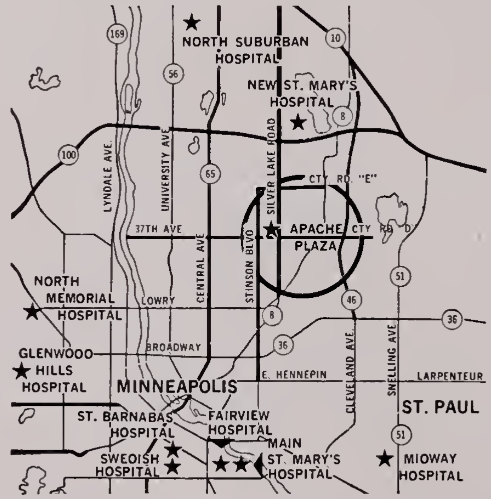
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Test Your Word Score

Watch for the asterisks in the manuscripts each month and test your word sense!

Akinesia — Weakness of motor function (page 854).

Scruple — 20 grains (page 879).

Drachm — 4.30 grams (page 879).

Autologic — self-directed (page 914).

Maladroit — Clumsy, gauche (page 914).

Athetoid — a condition in which there is a constant succession of slow writhing, involuntary movements of flexion, extension, pronation and supination of the fingers and hand, sometimes of the toes and feet (page 914).

Utopia — Greek ou (not) plus topos (place) (page below).

Coetaneous — contemporary (page below).

Beau monde — literally, beautiful world; by extension, worldly society (page below).

The Editor's Soliloquy

Utopia*

Utopia? — It is an ego-oriented society where everyone is free from illness, burdens, responsibilities, anxieties, apprehensions, worries; where the goods of life are available for the asking, where every man can have his cake and eat it, too, but no one need bake it; where rights and special privileges prevail without corresponding duties or onerous obligations, where a self-supporting government provides everything and demands nothing in return.

It is a society where the slogan "The Lord will provide" has been superceded by the expediency of "The Government will provide" without any *quid pro quo*; where the Jeffersonian ideal of independence has been abrogated in favor of parasitism. The paradox is obvious: as an individualistic society becomes more affluent, its humanitarianism impels it to ameliorate, if not eliminate inherent economic inequalities — only to discover too late that it has unwittingly fostered a bastard ideology of dependency.

Thomas More who coined the term, was not the only one who envisioned a nobler society. There were other Utopias: Plato's Republic, Augustine's City of God, Bacon's New Atlantis, and Campanella's City of the Sun: where only the virtues of human society prevailed; where there was no occasion to condemn, to blame, to censure; and where no vice existed — the nebulous felicity that always seems to pre-exist the coetaneous,* corrupt *beau monde.**

Carl O. Rice, M.D.

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*See Test Your Word Score above.

"All Registered Nurses are Alike"

It stands to reason. They all go through the same training; they all have to pass the same tests: they all have to measure up to the same standards. Therefore, all registered nurses are alike.

That's nonsense, of course. But it's no more nonsensical than what some people say about aspirin. Namely: since all aspirin is at least supposed to come up to certain required standards, then all aspirin tablets must be alike.

Bayer's standards are far more demanding. In fact, there are at least *nine specific differences* involving purity, potency and speed of tablet disintegration. These Bayer® standards result in significant product benefits including gentleness to the stomach, and product stability that enables Bayer tablets to *stay* strong and gentle until they are taken.

So next time you hear someone say that all aspirin tablets are alike, you can say, with confidence, that it just isn't so.

You might also say that all registered nurses aren't alike, either.

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Curbstone Consultation

Percutaneous Transhepatic Cholangiography

QUESTION: How often would you recommend transhepatic cholangiography in preference to cholangiography at the time of exploration or laporatomy?

ANSWER: The patient with what appears to be complete extrahepatic biliary obstruction constitutes a diagnostic problem. Percutaneous transhepatic cholangiography provides information that enables one to proceed rather directly with a definitive procedure. It has been particularly helpful to us in patients with stricture of the common duct, carcinoma of the ampulla of Vater, and cancer of the pancreas. If we really believed that the patient had a common duct stone, it is likely that we would not do a percutaneous approach, but do a cholangiogram at the operating table.

One of the great advantages of the percutaneous method is that it is done in the X-ray department with the many facilities that we do not have in the operating room. These include films taken from any angle, and cineradiography of the procedure. Also, we are sometimes able to demonstrate the dye entering either vascular or lymphatic channels.

Frank Glenn, M.D.
Cornell University Medical College

Spinal Cord Injury

QUESTION: I have recently witnessed the tragic consequences of spinal cord injury following aortography. Is there any way this complication can be avoided?

ANSWER: The following safeguards are suggested:

1. The contrast agent selected should exhibit the least nephro- and neurotoxicity. Currently 50-90% Hypaque is recommended.
2. The instillation of contrast material should be limited to a single injection.
3. If possible, the study should be carried out in the prone position.
4. The smallest volume of contrast material should be used commensurate with adequate visualization of the area being studied.
5. Some workers have suggested that barbiturate anesthesia should be avoided.

It is foolish to pluck out one's hair for sorrow, as if grief could be assuaged by baldness. — Bion

the problem: diabetic and overweight...unresponsive to diet alone

the answer: In the regulation of the diabetes "...if dietary control seems to be unsatisfactory...[and] if the patient is overweight...our first choice is phenformin [DBI], since this is the only oral hypoglycemic agent commercially available at present which does not promote fat deposit."[1]

"...with phenformin [DBI] there may be less preferential stimulation of fat synthesis in the obese, diet-resistant diabetic, favoring both blood sugar and body weight control."[2]

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DBI together with a proper diet usually affords effective control in the overweight ketoacidosis-resistant diabetic...reduces high blood sugar and elevated serum insulin levels, thus leading to gradual weight loss.[3] Anorexia has been suggested as a possible basis for weight loss. However, controlled studies suggest that it is due to the mechanism of drug action. Comparable dosages of DBI do not induce weight loss or lower blood sugar in non-diabetic subjects. For the ketoacidosis-prone diabetic, insulin is still the essential hypoglycemic drug.

Dosage: 1 to 3 capsules daily. **Side Effects:** Gastrointestinal, occurring more often at higher dosage levels, abate promptly upon dosage reduction or temporary withdrawal. **Precautions:** Occasionally an insulin-dependent patient will show "starvation" ketosis (acetonuria without hyperglycemia) which must be differentiated from "insulin-lack" ketosis which is accompanied by acidosis, and treated accordingly. Lactic acidosis has been reported in nondiabetics and diabetics treated with insulin, with diet, and with DBI. Question has arisen regarding possible contribution of DBI to lactic acidosis in patients with renal impairment and azotemia and also those with severe hypotension secondary to myocardial or bowel infarction. Periodic B. U. N. determinations should be made when DBI is administered in the presence of chronic renal disease. DBI should not be used when there is significant azotemia. Any cardiovascular lesion that could result in severe or sustained hypotension, which may itself lead to development of lactic acidosis, should be considered cause for immediate discontinuation of DBI at least until normal blood pressure has been restored and is maintained without vasopressors. Should lactic acidosis occur from any cause, vigorous attempts should be made to correct circulatory collapse, tissue hypoxia, and pH. **Contraindications:** Severe hepatic disease, renal disease with uremia, cardiovascular collapse. Not recommended without insulin in acute complications of diabetes (metabolic acidosis, coma, severe infections, gangrene, surgery). **Pregnancy Warning:** *During pregnancy, until safety is proved, use of DBI, like other oral hypoglycemic drugs, is to be avoided.*

Consult product brochure. **Also available:** DBI tablets 25 mg.

1. Faludi, G.: J. Am. Med. Women's Assoc. 18:722, 1963. 2. Weller, C. et al.: Scientific Exhibit, A.M.A., June, 1962. 3. Moss, J. M. et al.: Medical Times 92:645, 1964.

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Fracture–Trauma Conference

The Fatal Triad—Skull, Pelvis, Extremity Fractures

The combination of skull-pelvis-extremity fractures is particularly lethal to the patient involved in a high-speed automobile accident. It does not seem unusual that mortality and morbidity rates should rise with the number of body systems involved, but this particular combination carries with it a mortality rate that is disproportionately high. A recent review of such cases over a three-year period at the Hennepin County General Hospital revealed that only one out of four such injured patients survive their accident.

An illustrative case history of one such survivor follows:

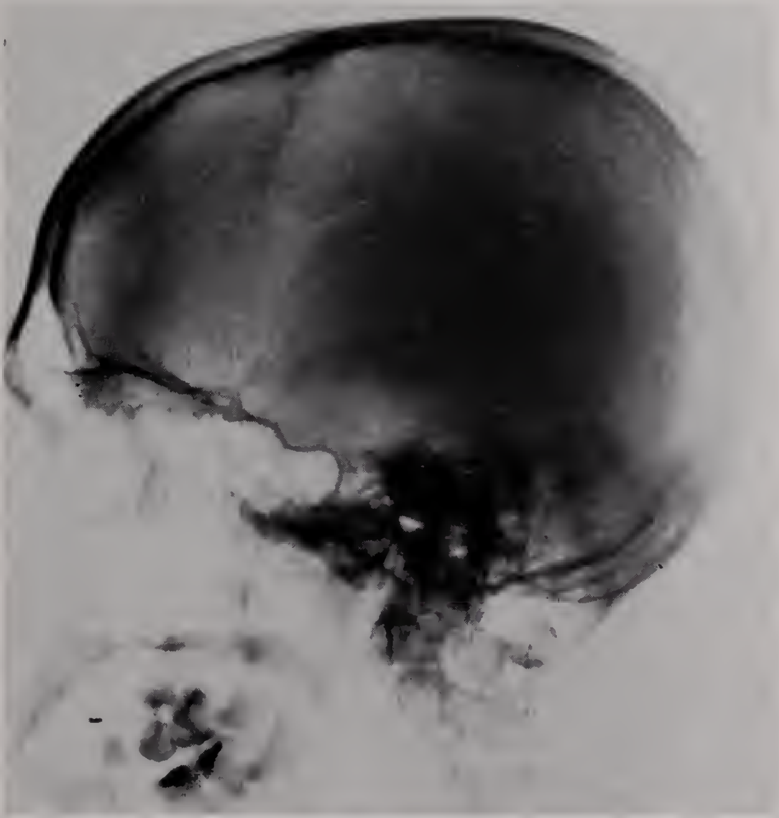

Figure 1

Continued

Case History

A 44-year-old pedestrian was struck down by an automobile and taken by ambulance to the Minneapolis General Hospital in a semicomatose condition. He was taken immediately to the emergency ward treatment room where he was evaluated.

He had an obvious head injury with a large area of swelling around the left ear and left temporal parietal area. He had also incurred a compound mid-shaft fracture of his left tibia and fibula. X-rays revealed a parieto-occipital linear nondepressed skull fracture (Figure 1), a severely comminuted left leg fracture (Figure 2), and fractures of the left superior and inferior pubic rami (Figure 3).

His initial blood pressure was 140/90, but his pulse was 116, and with a fall in the blood presure, blood replacement was started. He was disoriented, but neurological examination gave no evidence of localized intracranial hemorrhage. It was decided at this time to use a femoral sciatic regional block and treat the compound fracture. The block provided excellent anesthesia for the irrigation and debridement of the wound and insertion of a Lottes nail in the tibia. The patient remained awake during the procedure, although semistuporous, with no fall in blood pressure.

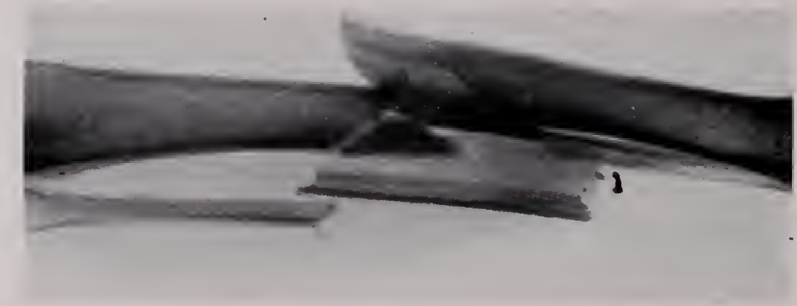

Figure 2

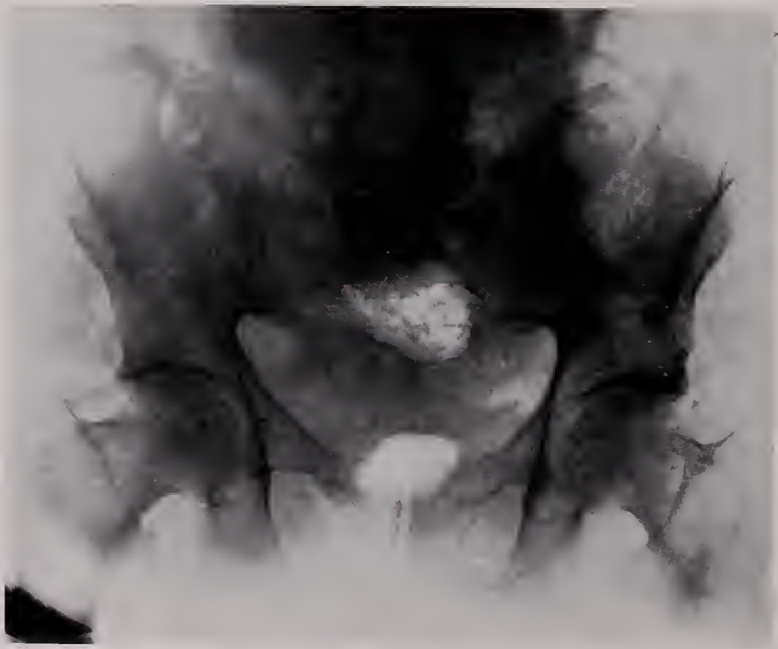

Figure 3

Postoperatively it was necessary to observe the patient closely because of an adynamic ileus, and nasogastric suction was instituted. He received seven units of blood over a three-day period until his hemoglobin had stabilized. There was no evidence of intra-abdominal organ damage. His recovery, thereafter, was rapid. His sensorium cleared and he was discharged home on the 19th post-accident day on crutches.

His last clinic visit was one and a half years later, at which time he was asymptomatic but walked with a slight limp. The fractures had all completely healed in satisfactory position.

Discussion

The physician who has the over-all responsibility for the care of such a patient must assume a heavy burden, for not only must he diagnose the separate injuries and see that they are properly treated, but he must determine the order of importance in terms of timing in correction. Several points seem worthy of consideration in the management of this difficult problem.

First, it is not uncommon that hypotension be present on the basis of retroperitoneal (hidden) hemorrhage resulting from the pelvis fracture. It is also not uncommon for the patient to be comatose from the head injury. A cause and effect relationship between the coma and the hypotension may lead to a false conclusion; if so, the patient may well exsanguinate without the proper blood replacement. This is a well documented fallacy but merits repeating.

Second, extremity fractures should be promptly splinted to prevent shock from pain and blood loss. However, definitive care can then be delayed, if the fracture is closed, until the patient's general condition has stabilized.

Third, if the extremity fracture is open or compounded, regional anesthesia may provide a good alternative to either a general anesthetic which causes added risk in the semicomatose patient or a spinal anesthetic in the patient who has only a partially compensated blood volume.

Fourth, should the neurosurgical consultant feel that there is reason for craniotomy, simultaneous definitive treatment of the extremity injury can frequently be accomplished with a consequent reduction in anesthetic time.

Summary

A case representing a favorable outcome from the frequently lethal combination of skull, pelvis, extremity fractures is presented. Experience with such cases had led to its being referred to as *The Fatal Triad.*

Harrison H. Farley, M.D.
Minneapolis, Minnesota

KLINEFELTER'S SYNDROME

The features of this syndrome include gynecomastia, small testes, aspermatogenesis without A-Leydigism and an increase in the excretion of follicle stimulating hormone. There is an increase in the follicle stimulating hormone comparable to castrates and a low normal level of 17-ketosteroids and estrogens.

If the disease starts in the prepuberal period, the typicals are a syndrome, but if it starts in the midpuberal period, it may be incomplete, though aspermia and sterility are always evident and varying degrees of eunuchoidism may be evident. Klinefelter's syndrome shows chromosome anomalies of the sex chromosomes. Any individual having immature or questionable genitalia should have a sex chromosome study, and if the clinical sex and the genetic sex are in confusion, chromosome studies should be done. — Robert H. Durham, M.D., Encyclopedia of Medical Syndromes, Paul B. Hoeber.

Paleopathology*

Paleopathology is that branch of physical science that deals with the antiquity of disease as revealed in the fossilized forms or the preserved remains of ancient organisms.

Fossils, however, supply data on only those diseases which leave their pathological record on the bones. Since tissues seldom become fossilized, the paleopathologist must remain largely ignorant of the majority of ancient diseases affecting the soft parts of the body.

There were doubtless epidemics among prehistoric animal species and early human societies that wiped out total groups; but as yet the relatively new science of paleopathology has accumulated no evidence of such fatal scourges. Future improved methods and techniques, however, may open hitherto closed doors to the archaic past to provide us with truer perspective on the evolutionary sequence and perpetuation of disease.

Fossil reptiles thus far studied give abundant evidence of five groups of pathologies: (1) arthridites (spondylitis deformans, multiple arthritis, and arthritis deformans); (2) tumors (osteoma and hemangioma); (3) necroses and caries; (4) hyperostoses (alveolar osteitis, exostoses, osseous hyperplasia, and osteoperiostitis); and (5) fractures (skull, oblique, simple, and caudal).

How did these various pathologies occur? The origin of fractures and some other injuries can be readily surmised; perhaps a rock fell on an animal or he was wounded in a struggle with another animal. The etiology of other skeletal pathologies, however, is more obscure; whether they were bacterial or tuberculous in nature has not been determined.

Had you been an ancient reptile with a well-and-smoothly-healed fracture, your good fortune could doubtless have been ascribed to two factors: first, your bones were solid, and second, your instinct of self-preservation impelled you to rest in an almost immobile position while you were recuperating — a therapeutic measure possible for you as a reptile, since you could survive for long periods without bestirring yourself to seek sustenance.

But since you possess neither armor nor a tail, your primate status would preclude a sufficient stretch of your imagination to identify with an ancient glyptodont** afflicted with necrosis of his bony armor due to the bite of a saber-toothed tiger, or with a dinosaur who developed a bone tumor overlapping two fractured caudal vertebrae.

On the other hand, you might easily identify with a Permian reptile whose infected spinal fracture resulted in osteomyelitis; or with a primitive mammal whose fractured elbow joint became ankylosed; or with a mosasaur† suffering from multiple arthritis in all joints of one hallux; or with a dinosaur whose oblique humerous fracture developed a subperiosteal abscess that permanently elevated his periosteum.

The animal pathologies described above were observed, photographed, and interpreted by Roy Moodie, Anatomy Professor at the University of Illinois, in his "The Antiquity of Disease," University of Chicago Science Series, 1923.

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*Paleopathology — paleo (old) plus pathology (disease).

**Glyptodont — a Pleistocene mammal related to the armadillo.

†Mosasaur — a Cretaceous marine reptile.

There are some remedies worse than the disease. — ***Publicus Syrus 42 B.C.***

Tumor Conference

Cystadenoma of the Pancreas

Cystadenomas of the pancreas are unusual benign neoplastic cysts. Approximately 100 cases have been reported in the literature.[8] In 1962 Piper, ReMine and Priestly of the Mayo Clinic reviewed the literature and reported an additional 20 cases.[7] Lichenstein in 1934 and Byrd in 1956 reported malignant degeneration in benign cystadenomas.[4,5]

These lesions are usually found in middle-aged females. They may occur in any portion of the pancreas but are generally in the body and tail. They may vary greatly in size when discovered; tumors varying in size from 2 x 2½ cm. to 34 x 20 x 20 cm. have been reported. Pseudocysts, however, are usually larger than cystadenomas.

Etiology

Numerous theories of etiology have been reported. Glenner and Mallory concluded that cystadenomas originate from proliferating pancreatic duct epithelium.[1]

Gross

The tumors are embedded and often replace pancreatic tissue. They have a profuse blood supply with large blood vessels coursing over the surface. They are firm and nodular, grossly appearing as a cluster of grapes, and on section resembling a honeycomb. There is no communication between the cysts or with the main pancreatic duct. The cysts contain a viscid, mucoid, gelatinous or clear serous fluid.

Microscopic

The cysts are lined by a single layer of epithelium. The cytoplasm is clear, the nucleus basal. The cells may be flat, cuboid or columnar. The fibrous stroma between the cells may contain calcium or show evidence of hyaline degeneration. The surrounding pancreatic tissue may be normal or show evidence of compression.

Symptoms

The symptoms are those of a slow-growing lesion. In most instances the

Continued

only symptom may be that of a palpable abdominal mass. Occasionally, a patient may complain of fullness, or a sensation of pressure when bending over. There may be anorexia, constipation, or nausea and vomiting. The tumor may be found during abdominal exploration during other abdominal surgical procedures. Diabetes co-exists in 10 to 14% of reported cases; but diabetes has not been reported as a complication following surgery.[6]

Findings

A firm, round, nodular, nontender upper abdominal mass is the usual clinical finding. If the lesion is in the tail it may move with respiration. There is no movement if it is in the head of the pancreas. On roentgenography, an anterior abdominal mass may be seen, with evidence of extrinsic lesion pressing on the stomach or colon. Scout films and pyelograms help make the differential diagnosis. Calcific deposits have been noted on 15-20% of these cysts.[2]

Diagnosis

Clinical, radiographic and laboratory findings may not be specific enough for a definite diagnosis to be made preoperatively; but the existence of a relatively asymptomatic solid upper abdominal tumor in a middle-aged female should suggest the diagnosis.

Treatment

Surgical extirpation of the tumor is indicated. Marsupilization or internal drainage is not effectual, as the cysts do not communicate.

The tumor is approached through the gastrocolic omentum. Usually a

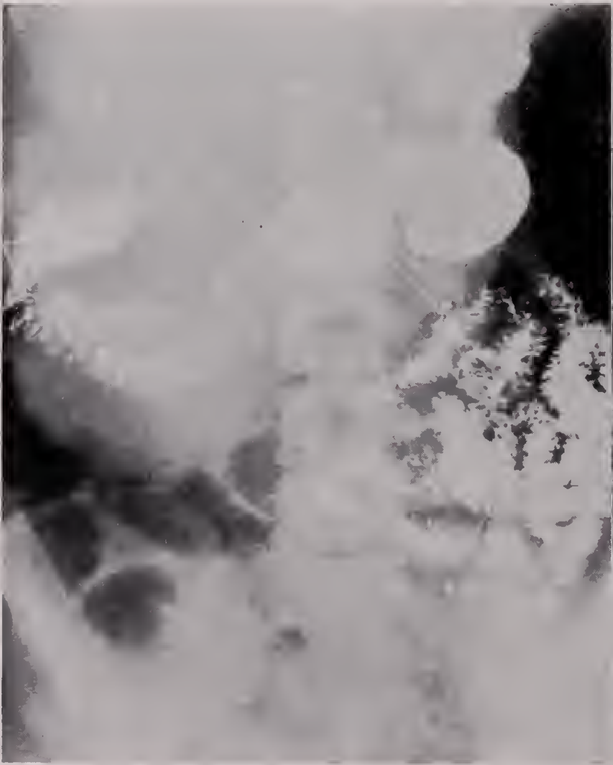

Fig. 1 — Displacement of the stomach and widening of the duodenal loop, with downward displacement of the gas-filled colon due to the tumor.

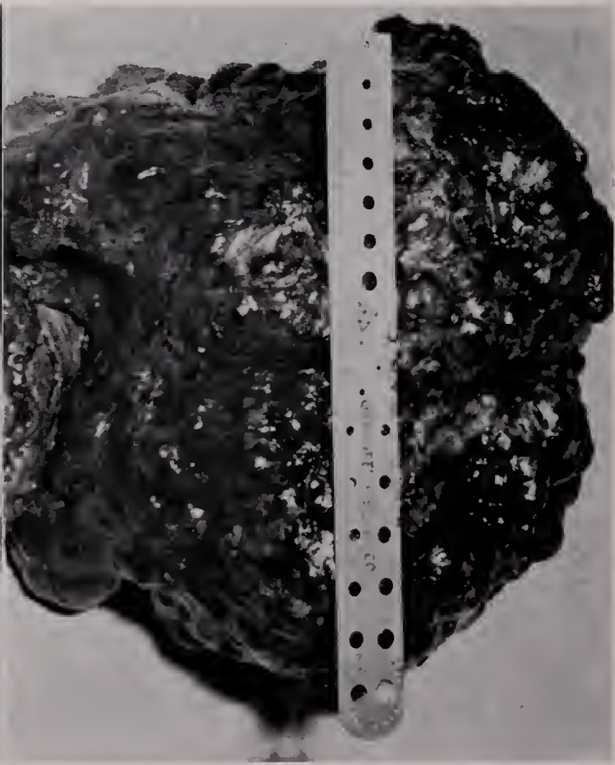

Fig. 2 — The gross specimen showing multiple cysts.

good cleavage plane can be found; but the cyst may be covered with a thin layer of pancreatic tissue. Most of the tumors are in the body and tail; if in the tail, the spleen is removed with the tail of the pancreas. Care must be taken to avoid the superior mesenteric vessels and the portal vein. If the cyst is in the head, as much pancreas as possible is preserved; and particular attention must be paid to the pancreatic and bile ducts. The preservation of even a small amount of pancreatic tissue prevents the development of postoperative diabetes. Howard believes the operative mortality rate should not exceed 2-5%.[6]

Case Report

A 54-year-old woman had consulted her physician ten years previously for a nontender upper abdominal mass. This was thought to involve the upper pole of the kidney, and she was explored through a right subcostal incision. At surgery the mass was found to be a multicystic lesion involving the pancreas. It was felt, after consultation, that removal of the mass through the renal incision would be unwise, and the wound was closed. Following surgery the nature of the lesion was explained to the patient, and removal through a transabdominal incision was advised. The patient, however, declined further surgery at that time.

She had few symptoms and continued to postpone surgery. In February of 1963 she noted a mucous discharge from the rectum. A carcinoma of the rectum 15 centimeters above the anal verge was found on sigmoidoscopy. A massive hemorrhage followed proctoscopic biopsy. After transfusion, an anterior resection of the rectosigmoid was done. The upper abdomen was explored at the time of surgery and a large, multilocular cyst occupying the major portion of the upper abdomen was found. The duodenum was stretched over the mass. The pancreatic lesion was not disturbed. Following the bowel resection a fecal fistula developed, and a temporary colostomy was done. The colostomy was closed six weeks later.

The patient did well postoperatively but began to have abdominal discomfort after meals.

One year later, after careful clinical and roentgenographic examination revealed no evidence of recurrence of the rectal carcinoma, she was ad-

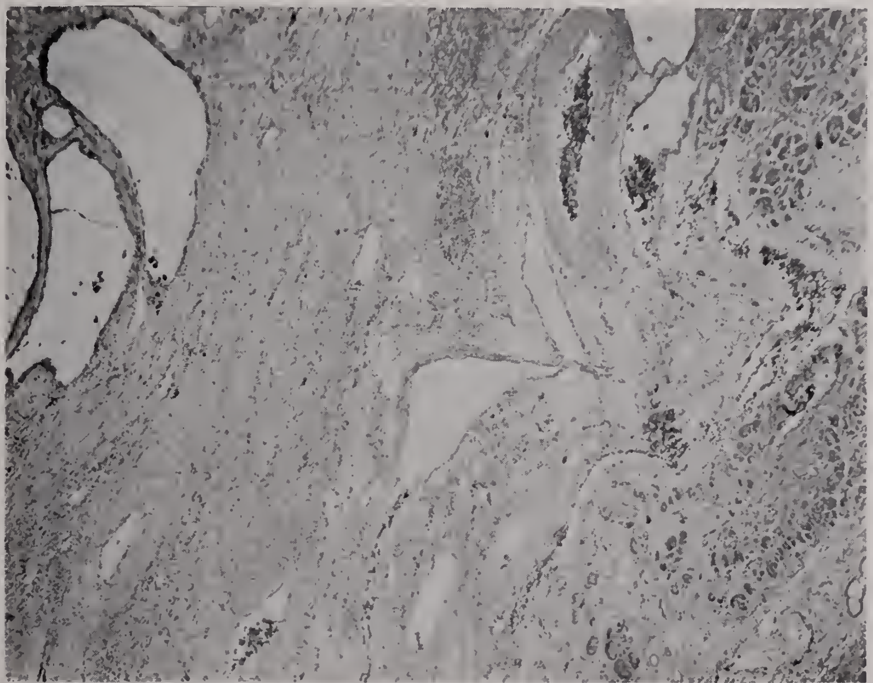

Fig. 3 — Microscopic section showing the dense fibrous stroma with trabeculations and cystic areas.

Continued

mitted for surgical removal of the pancreatic cyst. A right and left subcostal incision was made. The gastrocolic omentum was taken down, exposing the body and tail of the pancreas. The very large tumor was apparently confined to the head and uncinate process of the pancreas, as there was no tumor to the left of the mesenteric vessels. The vessels were pushed to the left and the duodenum to the right, as the tumor measured 20 cm. x 14 cm. x 9 cm. The common duct was transected above the tumor, and 10 centimeters of the second portion of the duodenum resected with the cystadenoma. There was no identifiable duct system left in the small, atrophic-appearing tail of the pancreas. The common duct was anastomosed to the duodenum and the duodenum reapproximated, with a T-tube in the common duct, one limb extending thru the choledochoduodenostomy. Penrose drains were placed in the area of resection and the abdomen closed.

On gross examination of the tumor numerous cysts of various sizes were seen protruding from the surface. The cysts had a smooth inner lining and contained a thin clear, or serosanguinous fluid. No papillary tumor was found. Throughout the specimen, areas of fibrosis and even calcification were found. The pancreatic tissue could be identified.

On microscopic examination the stroma was found to be a dense fibrous tissue, which resembled scar tissue and formed an intricate pattern of trabeculations that varied in thickness and density. A few of the cysts lacked an epithelial lining, but the majority were lined with a single layer of cuboid epithelial cells. There was no evidence of epithelial activity.

A few areas of pancreatic tissue were found; in some areas the pancreatic tissue was considerably compressed. The islets of Langerhans appeared to be normal.

On the first postoperative day the patient had glycosurea and a blood sugar of 157 mg. per 100 cc. of blood. On the following day there was no glucosurea, and her blood sugar remained normal. Her convalescense was uneventful; she was discharged from the hospital on the fifteenth postoperative day. Her T-tube was removed four months later.

She has continued to do well, has maintained her weight, and has shown no glucosurea. Her fasting blood sugar analysis has been reported within normal range.

Summary

A case of large benign cystadenoma known to exist for 10 years of the pancreas is reported. It was surgically excised, with a small amount of pancreas preserved. Postoperative diabetes did not develop.

E. Theodore Palm, M.D.
Horace G. Scott, M.D.
Minneapolis, Minnesota

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6-8 May be obtained from the author or in the reprints.

Neuro-Pediatrics Conference

Phenylketonuria*

Seven-Year-Old Female Presenting with a School Learning Problem and Incoordination

Dr. David Piepgras:**

This seven-and-one-half-year-old white female was referred to University of Minnesota Hospitals by Dr. Paul Meyer of Faribault, with the possibility of muscular dystrophy. The mother felt that the patient's problem was primarily "stiffness on getting up in the morning, incoordination at play, and holding her pencil funny."

The child is the product of a full-term normal delivery, weighing six pounds, seven ounces at birth. Her development shows that she held her head up at one month, rolled over at three to four months, sat at five and one-half months, walked at 15 months, and said single words at 12 months. The mother states that her development was slow compared to that of her other children.

Approximately one year ago the mother observed that the child had a "coordination problem" when she became overly tired. In school it was noted that she had a short attention span and trouble with writing; her words ran together and her letters were of varying sizes. However, her school performance had previously appeared to be quite satisfactory. In the preceding six months her teacher had remarked that the patient ran "funny" and had apparent trouble in starting to run, as she appeared "stiff-legged." It was also noted that her "legs are stiff in the morning and she has trouble descending stairs and holding things in her hands," especially her fork and her pencil. These symptoms are more noticeable when she is tired and are not associated with weakness.

The review of symptoms shows that she had severe eczema from two months to two years of age and is allergic to penicillin. She has had no convulsions, irritability, excessive vomiting or other neurological symptoms.

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*See Phenylketonuria in Minnesota: Minnesota Med 47:501, 1964.

Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatrics conferences are held the first and third Wednesdays of every month from 1:00 to 2:00 p.m. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Robert W. ten Bensel, in Pediatrics, and Dr. Robert Soll, in Adult Neurology.

Conference held on January 6, 1965.

**Senior Medical Student, University of Minnesota.

Continued

The mother is 35 years of age and the father 32. The parents were divorced four years ago and the patient is the only child by this marriage. The mother has two children by a subsequent marriage, who are both apparently normal. The paternal grandfather died of "muscular dystrophy" at age 50. There is no other documented history of neurologic disease in the family.

The patient lives with her mother, step-father and two step-sisters. The family group interaction is not well known as the mother rarely talks about the family, even on direct questioning.

Physical examination shows an obese (94-pound), alert and pleasant white female with brown hair and hazel eyes. Vital signs are normal. Examination of the eyes, ears, nose and throat is normal. No heart murmur is heard and no masses felt on palpation of the abdominal wall. Neurological examination shows no motor weakness and good muscular strength. Her reflexes are bilaterally equal, and there are no pathological signs. Her Romberg is negative and her gait somewhat wide-based, with her feet rotated externally; but she has a steady gait.

The initial impression was that the child may be having an adjustment reaction to family stress.

Laboratory work, including a white count, urinalysis and Mantoux, was negative with the exception of a positive ferric chloride test.

Dr. Paul Moe:*

The patient is observed to be a pleasant child, but somewhat nervous and maladroit** in her movements. Neurological examination shows normal cranial nerve function and a head size of 51.5 cm. (normal). Her reflexes are symmetrical and somewhat hyperactive. There is questionable athetoid** posturing drift of the left arm. Serum muscle enzymes, drawn because of the family history of muscular dystrophy, were all within normal limits. Another ferric chloride test was performed and was strongly positive. A blood phenylalanine level was 45 mg. per cent.

Mr. Art Straub:†

Presently the patient weighs 101 pounds and is 51 inches tall. Her incoordination, which was very evident six months ago, as manifested by her not being able to write between lines, is now diminishing. Her nervousness is also decreasing, and she is described by her teacher as "cooperative, willing, even-tempered, happy and friendly." Her work is still in the low average range, has an unorganized quality and is somewhat "messy;" but she stands sixteenth in a class of twenty-two. When given a multiple choice situation it is difficult for her to make a decision. She seems to demand and receive a great deal of attention from her teacher; directions frequently need repeating before she is able to carry out a task. She used to talk a great deal to herself; now she indulges less in this autologic** habit. A good mother-child relationship appears to be present, as the mother and patient are doing exercises in an attempt at weight reduction.

Generally, the school feels that she is producing satisfactory work and

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*Pediatric Neurologist, University of Minnesota Hospitals.

**See Test Your Word Score Page 901.

†Principal, Lincoln Elementary School.

Continued

has a feeling of success. She is particularly interested in music and has a good voice. She does stand out in her class because of her large size and her incoordination, and this is what prompted the initial evaluation by Dr. Meyer, who subsequently referred her to the University.

Mr. Earl Schramm:*

This child will remain in a regular school class as long as this is feasible and her academic work progresses satisfactorily. Faribault has special education classes in the grade school, junior high school and senior high school. At the present time, there are two sections in the grade school, but I feel that these are not now indicated because of her satisfactory progress at the present time.

Dr. Harold Ireton:**

On psychological testing performed at the Lincoln School in March, 1963, she scored an I.Q. of 74 on a Stanford-Binet. Testing in July, 1964, at the University of Minnesota Hospitals indicated significant intellectual impairment. A measure of the verbal intelligence (Wechsler Intelligence Scale for Children) plus the child's talkativeness suggested an average intelligence (verbal I.Q., 94). However, other clinical and test evidence suggest that she may not be capable of functioning at this level. Clinically she appears highly distractible. In tests of spatial relationships and visual motor coordination, she does relatively poorly (WISC performance I.Q. 71, inferior Bender). She has exceptionally poor recall. Such a pattern of functioning suggests a brain-injured child, and her hyperactivity would predict learning difficulties in a standard school situation.

While it has been reported that she has fair success in school, a reading problem has been noted. The results of the above evaluation point to increasing difficulty in school and the need for special class education or special attention to take account of her deficits. The question must be raised as to whether the improvement she has made in the past four months is apparent or real; it could be misleading and bar her from receiving the special help she is certainly going to need.

Mr. Straub:

Her reading has improved this past year, and a reading achievement test performed in the second grade showed a score of 1.9 grades. Small class size and individual attention certainly may be a factor in her improvement.

Dr. Robert Fisch:†

We would expect no further intellectual deterioration, as children with phenylketonuria at this age remain stable. Brain damage occurs in the first two years when the brain is maturing at a rapid rate.[1]

I was told after the first visit that this patient had normal intelligence; however, a personal interview with mother and child revealed that the child had borderline low intelligence. Therefore this case is particularly interesting because of the patient's relatively high I.Q. for an untreated phenylketonuric. Phenylketonuria is quite rare, affecting 1/20,000 to

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*Director, Elementary Education.

**Psychologist, University of Minnesota Hospitals.

†Pediatrician, Director, Phenylketonuric Clinic, University of Minnesota Hospitals.

Continued

1/10,000 children born. Only two cases have been reported with I.Q.s greater than 110, and only one per cent of the untreated patients have borderline normal intelligence.[2]

Unfortunately, we very often see that parents and even physicians overlook the slow development of children; and when school failure calls attention to the borderline brain-damaged child, the time is rather late for significant correction of the pathological condition. This patient had early, slow development by comparison with her siblings. Besides, the presence of eczema, often seen in phenylketonuria,[3] should have instigated an early diagnosis.

The implications of the diagnosis are several. First, in terms of genetic counseling to the family, early diagnosis is extremely important, since recessive inheritance is involved and there may be other children affected. The two half-siblings of the patient have been tested and found to have normal phenylalanine blood levels. Genetically, the divorce of the mother was a fortunate, preventive measure.

The question is now raised as to whether low phenylalanine diet may be of benefit to this patient. There is evidence that there may be improvement of symptoms in severely affected untreated phenylketonurics. A case illustrating this point is that of a 12-year-old boy who, after four months on the diet, showed marked improvement in his writing ability (Figures 1 and 2). One of the main factors to consider in placing an older phenylketonuric on the special diet is that the diet requires a great deal of patient parental effort because it is unpalatable and restricted. The cost is also somewhat prohibitive in some cases; for a patient six to 12 years old this usually runs from $60 to $120 a month.* On the basis of intelligence alone, Jervis[4] has stated that the diet is of no benefit after three years of age; therefore, at the present time I do not feel that diet is indicated for this child.

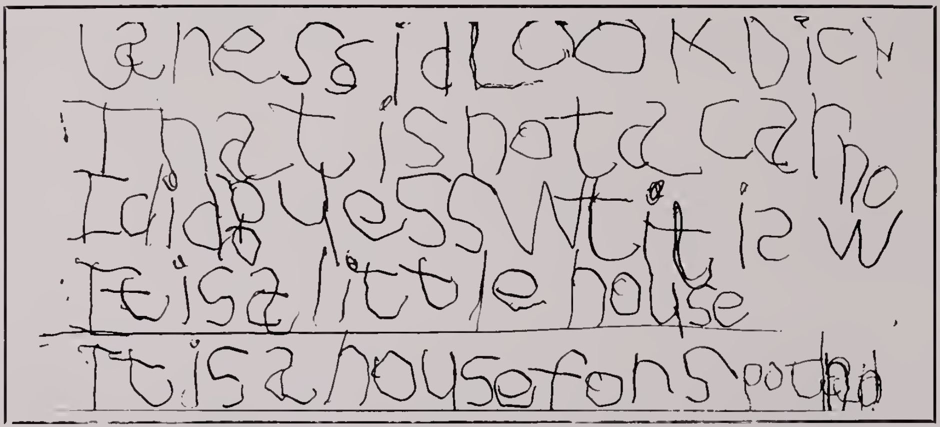

Fig. 1 — Handwriting of a 12-year-old untreated phenylketonuric child before low-phenylalanine diet.

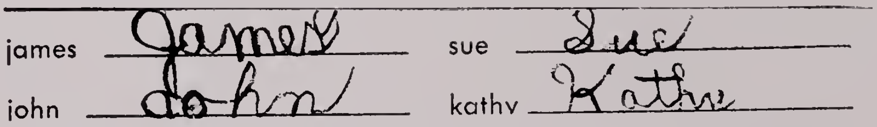

Fig. 2 — Handwriting sample after four months of low-phenylalanine diet.**

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*The expense of the formula can be tax deductible. The expense depends upon the amount of formula needed and the different price charged through pharmacists.

**Photographs courtesy of Dr. Robert Fisch.

As this patient becomes older and approaches the child-bearing age, pregnancy would be an indication to start the diet. There is data to suggest that high phenylalanine in the mother's serum may be a cause of mental retardation. The obesity which this child shows has also been seen in some untreated phenylketonurics; the reason for this is unknown. Most of the children, however, who are on the diet, belong to the lower weight group for their age.

This family is of low economic status and it is difficult for them to keep appointments and meet obligations. For this reason, a complete evaluation has not been made, such as an electroencephalogram and skeletal survey. Hopefully, it may be possible in the future to obtain money from a research grant for further studies as they are indicated.

This patient will provide a case for observation and a standard for comparison until better testing methods are devised for psychological testing of phenylketonuric children. There is no necessity for her to return to Phenylketonuric Clinic before this summer. The school situation is certainly adequate at the present time; but the patient should have yearly psychometric examinations.

Dr. Heinz Bruhl:*

This case is indeed very interesting and points out the need to screen for phenylketonuria older children who have minor neurological abnormalities and/or school difficulties. This may lead to recognition of families in which the abnormal gene might not otherwise be discovered.[5] Knox[6] reported 20 untreated phenylketonurics with I.Q.s of over 60, and there are in the literature approximately 25 cases with I.Q.s of over 70. In Minnesota, there are a substantial number of phenylketonurics: 56 at the State Hospital in Faribault and 52 at the University of Minnesota, whom Dr. Fisch is following.

At Faribault State School we have tried the low phenylalanine diet on ten older phenylketonuria patients on a control basis for five years.[7] The diet produced favorable somatic changes, including improvement of skin conditions, decreased muscular rigidity, better coordination and motor functions. However no significant improvement in intellectual ability was produced. This study makes it imperative that phenylketonuria be diagnosed within the first few months of life before permanent and irreversible brain damage has occurred.

Final Recommendations of the Conference

1. Dr. Meyer will maintain primary medical responsibility in this case.
2. Communications will be maintained by Dr. Fisch with Dr. Meyer and the school officials regarding any recommendations about therapy or counseling.
3. The family should be encouraged to seek help from the County Welfare Board if borderline economic status precludes adequate medical care.
4. Psychometric testing should be performed at yearly intervals by the school or at the University of Minnesota Hospitals.
5. Consideration should be given to the patient as a growing child,

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*Pediatrician, Faribault State School for the Retarded.

Continued

especially in regard to her obesity problem. Dr. Meyer should work closely with the family in attempting a weight reduction program.

Robert W. ten Bensel, M.D.
University of Minnesota Medical Center

Those Participating in the Conference: Dr. Paul Moe, Pediatric Neurologist; Dr. Robert Fisch, Pediatrician; Dr. Heinz Bruhl, Pediatrician, Faribault State School for the Retarded; Mr. Earl Schramm, Director, Elementary Education, Faribault, Minnesota; Mr. Art Straub, Principal, Lincoln School, Faribault, Minnesota; Mrs. Mary Cordingley, Social Worker; Dr. Harold Ireton, Psychologist; Dr. Robert ten Bensel, Moderator.

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Surgery Comes into Its Own

The surgeon entered the new century (the Twentieth) as someting of a popular hero, a man henceforth destined to share the not-always-welcome limelight turned on him by an inquisitive press. In the popular mind his prestige had begun to outweigh that of the physician. Here was a man who had as much skill and subtlety in his fingers as a great violinist, a brain as cool and calculating as a general's. When lesser men were still yawning at their office desks in the morning, the surgeon was displaying courage, subtlety, strength and judgment at an operating table, recovering not only tin whistles from the stomachs of children but bullets from the skulls of policemen. Of course he soaked the rich (and good luck to him!) but he remained faithful to the old tradition of aiding the poor for nothing. What greater stature could a man desire? What higher satisfaction than to see, happily going about their lawful occasions, men and women who but for his intervention would assuredly have been six feet underground?*

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*Turner, E. S.: Call the Doctor. St. Martin's Press Inc., New York, 1959, p. 242.

ANSWER TO WHAT'S YOUR DIAGNOSIS

(From page 884)

Skin lesions appeared progressed to the characteristic appearance of herpes zoster. The burning distress across the abdomen and the costo vertebral tenderness should have led to the suspicion of herpes zoster.

Physicians ought to console their patients even if the signs of impending death seem to be present. For the bodies of men are dependent on their spirits.

— Rhazes (865-925)

Cytogenetics Laboratory Services

The Minnesota Department of Health announces the establishment of a Cytogenetics Laboratory to aid in the identification of specific diseases with chromosome anomalies. This new service will be under the joint sponsorship of the Human Genetics Unit, Division of Special Services, and the Virus Laboratory, Division of Medical Laboratories.

Since the discovery in 1960 that Down's Syndrome (mongolism) was associated with the occurrence of an extra chromosome (trisomy 21), a number of diseases and syndromes have been found to exhibit chromosomal irregularities. (Kleinfelter's* and Turner's syndromes are two which show chromosome anomalies of the sex chromosomes, and there are many variations of these anomalies that have been reported.) Any individual having immature or questionable genitalia should have a sex-chromatin study done (i.e., determination of the presence or absense of sex chromatin in the nucleus of squamous epithelial cells), and if the clinical sex and the genetic sex are in confusion, chromosome studies should be done.

There are two syndromes which have been described (Trisomy 13-15 and Trisomy 17-18) in which the patients show multiple congenital anomalies specific for each of the two syndromes. While chromosomal anomalies are rare it is estimated that they are associated with about 10 per cent of all congenital malformations, about five to ten per cent of mentally defective children, and one per cent of sterility.

Procedure for Cytogenetics Laboratory Services

The Cytogenetics Laboratory will provide chromosome karyotyping for diagnostic purposes, upon referral from physicians, dentists, and health agencies, at no charge. Because of the limited number of patients which can be examined, all referrals will be screened through the Human Genetic Unit and priorities set.

1. Referrals should be sent in writing to the Human Genetics Unit, Minnesota Department of Health, and should contain all pertinent medical history, tentative diagnosis, and the reasons for requesting chromosome karyotyping.

2. The physician or agency will then be notified of the priority for this patient.

3. Arrangements will be made with the physician to obtain the required 10 cc. heparinized peripheral blood specimen from the patient. (Collecting tubes will be provided by the Department of Health.) Because cell culturing becomes difficult when the sample is over six hours old, it may be necessary for patients living any distance from the Twin Cities to have the specimen drawn in the Twin Cities.

4. Due to the culturing procedures for chromosome karyotyping specimens will be accepted only on Monday or Tuesday of each week.

5. Upon completion of the karyotyping a written report will be sent from the Human Genetics Unit to the referring source, two to three weeks after submission of the specimen.

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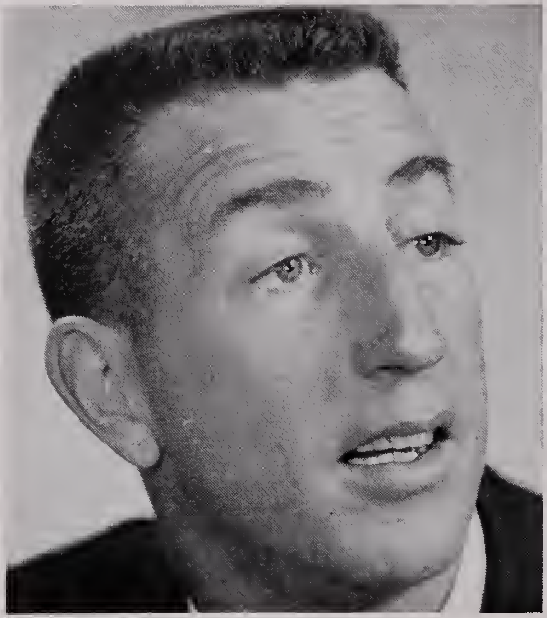
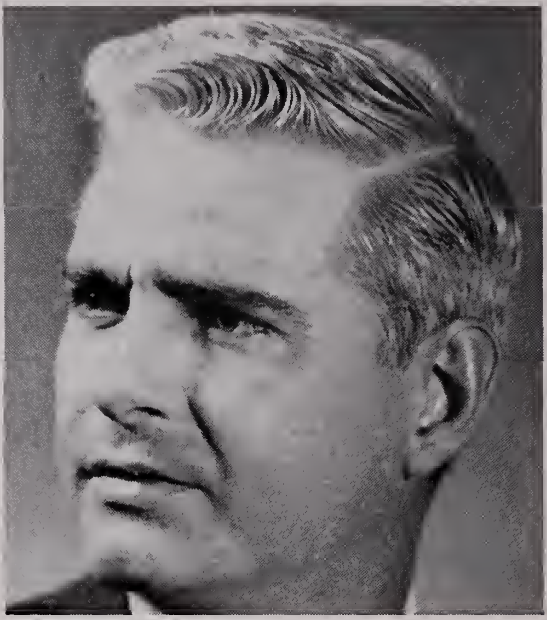
*See Page 907.



F. P. Tolan, Jr.—St. Paul-Rochester



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Grand Rounds

The Use of Extracorporeal Dialysis*

(Artificial Kidney)

Several means for removal of circulating products of metabolism from the blood are available — gastric lavage, irrigation of an isolated loop of ileum, high colonic lavage, pulmonary lavage, and peritoneal dialysis.[1] All of these are less efficient than the artificial kidney. Some patients may be better suited to peritoneal dialysis which, therefore, may not be in direct competition with hemodialysis.[2] Peritoneal dialysis may be a better choice in:

1. Coagulation defects (i.e., thrombocytopenia)
2. Active gastrointestinal bleeding
3. Those without accessible vessels
4. Those with rare blood types
5. Small children and infants

In addition, peritoneal dialysis is easier, requires less personnel for maintenance and does not require a trained team or elaborate mechanical equipment. With the use of regional anticoagulation, active gastrointestinal bleeding is no longer a contraindication to artificial kidney hemodialysis.

Development of an effective therapeutic agent is based on a biphasic process. The first phase entails the development and refinement of a particular technique free from dangers and side effects. This is followed by the second phase — that of clinical application — which demands a knowledge and appreciation of the factors indicating the use of the technique.

The first phase of hemodialysis commenced in 1914 when Abel et al.[3] postulated that, in renal failure, accumulated waste products could be removed by means of dialysis outside the body. The advent of "cellophane" as a satisfactory semipermeable membrane and the discovery of heparin enabled Kolff to develop the first artificial kidney for clinical use in 1944. The period since World War II has seen a tremendous number of improvements and developments in the technical and engineering aspects of these machines. The first phase is completed in the sense that the technique and performance of hemodialysis are no longer in the experimental stage, and

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*Presented as a Medical Grand Rounds at Mt. Sinai Hospital, Minneapolis, January 26, 1965.

Continued

the procedure is virtually free from any serious dangers. The routine use of hemodialysis in clinical practice has also now been firmly established.

Concept of Urea Balance

The continuous formation of urea requires its removal by the kidneys. There is, therefore, a balance between its production and removal (Figure 1).[4] When this balance is upset, accumulation of urea in the blood results. This imbalance can be the result of (1) decrease in urinary output or (2) increase in urea formation. Figure 2 is a schematic representation of the possible events when this balance is upset. The normal balance is depicted by the position of the axis A-A′. A minor upset (B.B′), provided it does not go outside the block abcd, can usually be handled by normal body compensatory mechanisms. The block abcd, is, therefore, representative of the compensatory state. However, when the upset in the balance is such that it passes out of the confines of this block (say to C-C′), treatment becomes important in order to interrupt the progression to D-D′, which is equivalent to death. The rate at which the change in position from A-A′ to C-C′ occurs influences the ultimate prognosis. Therefore if, in the early stages of renal failure, the daily rise of the blood urea level is rapid, immediate dialysis should be considered. It is the daily rise in blood urea level, rather than the absolute blood urea level, that governs the selection of patients for hemodialysis.

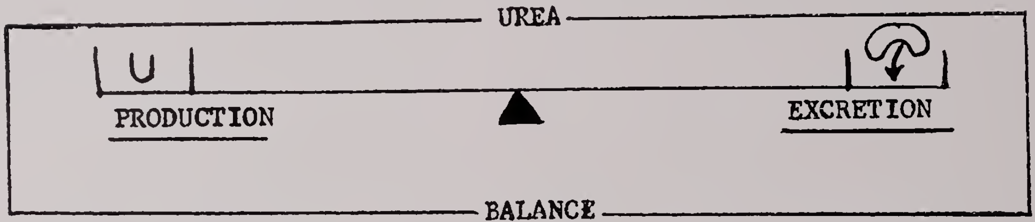

Fig. 1 — (After Nayman, 1962)

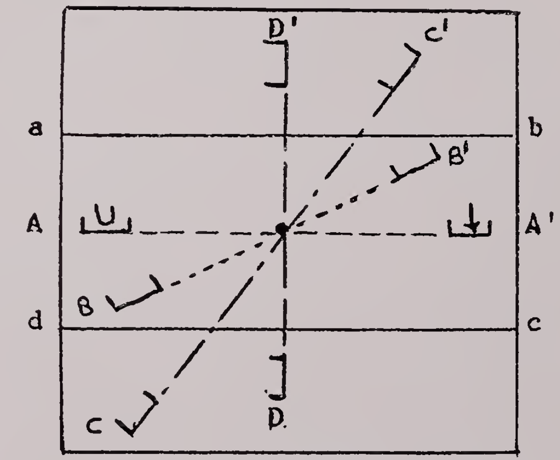

Fig. 2 — (After Nayman, 1962)

Increased Production

An increase in protein catabolism and urea production can be due to (1) trauma, (2) surgery, and (3) infection. The formation of urine is dependent upon adequate renal blood flow, glomerular filtration, tubular secretion and absorption and patency of the conducting channels to the exterior. The glomerular and tubular factors constitute the renal element, and the blood flow and conducting channels constitute the extrarenal elements.

Decreased Excretion

The causes of decreased excretion of urine are either renal or extrarenal. Renal causes are: (1) glomerular disease and (2) tubular necrosis. Extrarenal causes are: (1) inadequate renal blood flow and (2) lack of patency of conducting channels. The tubular lesion (acute tubular necrosis), trauma, surgery, sepsis, acute glomerulonephritis and reduction in renal blood flow constitute the acute lesions. Chronic glomerular disease and the uropathies are responsible for the chronic lesions.

Any of the above factors, alone or in combination, can cause renal failure, of which an elevated blood urea level is merely an isolated and single manifestation. The interplay of these factors is indicated by the concept of urea balance, and urea imbalance is an index of the factors constituting the derangement of renal failure.

Different Types of Artificial Kidneys

Abel's apparatus[3] consisted of a set of cylindrical collodion tubes through which blood from dogs could flow. The tubes, enclosed in a chamber, were bathed in saline. Hirudin, extracted from the heads of leeches, served as the anticoagulant. The collodion acted as a semipermeable membrane through which substances of small molecular weight were removed from the blood by dialysis. Quantitatively the results were poor; part of the difficulty was the thickness of the membrane.

Necheles in 1923 constructed an artificial kidney using sheep's peritoneum as the dialysing membrane. Haas in 1925, still using hirudin as the anticoagulant, first attempted dialysis of a human being; but the amount of urea removed was small.

A few attempts have been made to construct artificial kidneys from ion-exchange resin columns, but these have been only partially successful.

The four types of machines which have proved their efficiency over the course of time are the Kolff rotating drum, Alwall, Skeggs-Leonards and the Kolff twin-coil disposable kidneys.

Kolff Rotating Drum

Not until 1944 did Kolff and Berk, working in German-occupied Holland, first report on the successful use of an artificial kidney to remove significant amounts of urea and other catabolic products from patients with renal failure.[5] Blood from the patient flowed through cellophane tubing which was wrapped around a large rotating drum partially immersed in a physiological salt solution, the dialysate. Similarly constructed kidneys are still in use.

The Kolff rotating drum kidney has been modified by increasing the size of the drum and the rinsing bath, and the time of the dialysis has been reduced to 4½ hours. It is accepted that the more efficiently the dialyser unit is capable of reducing the time of the dialysis, the less the procedure-fatigue to the patient and the less time-consuming for the staff. However, it has also been shown that sudden and rapid alteration in the tissue

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electrolytes can produce a deterioration in the condition of the patient, and it is better to limit the time of these more efficient dialyses rather than attempt to complete urea clearance.

In the Kolff type of kidney there is a build-up of electrolytes in the dialysing fluid bath over the course of the dialysis, and the dialysis is stopped every two hours to replace this fluid with a new solution.

Alwall

In 1947, Alwall in Sweden developed a functional kidney consisting of cellulose tubing wrapped around a wire net and enclosed by a second wire net.[6]

The lower over-all efficiency of the Alwall kidney is a serious handicap in treating patients in whom the blood urea rises rapidly between the dialyses. Alwall has compensated for the lower clearance of his machine by prolonging the time of each dialysis.

Skeggs-Leonards

In contrast to the coil kidneys are the parallel flow units. Here blood flows through several short lengths of cellophane membrane arranged in parallel. Such an arrangement offers much less resistance to blood flow, making it possible for the patient's own arterial pressure to propel blood through the system without the use of an accessory pump. Examples in use are the Skeggs-Leonards,[8] Kiil[9] and macNeill-Collins[10] dialyzers.

The Skeggs-Leonards kidney differs from the Kolff rotating drum and twin-coil disposable artificial kidney in that there is a continuous flow of blood and dialysing fluid in opposite directions for the full six hours of dialysis. Consequently, it is not necessary to stop the machine during the course of dialysis. The composition of the dialysing fluid is not altered during the time of dialysis, the fluid in the dialyser being continuously replaced by fresh dialysing fluid containing a constant concentration of electrolytes.

Kolff Twin Coil

The disposable twin-coil kidney which is presently in widespread use in hospitals throughout the world was developed by Kolff and Watschinger in 1956. The coil consists of two flattened cellulose tubes, each 10.75 meters long, enveloped in fiberglass screens and wrapped around a central cylinder. The coil is placed in a 100-liter tank containing the dialysate which is pumped up through the fiberglass screens. Arterial blood from the patient flows through the cellulose tubing, assisted by a pump, and then returns to a vein. Dialysis takes place in the coil. The dialysate consists of physiological concentrations of $Na+$, $Cl-$, $K+$, $Mg++$, $Ca++$, $HCO3-$, lactate and glucose in water. It is changed every two hours during the average six-hour "run".

Capacities of Dialysing Units

The volume of blood required to prime the dialysing unit is of considerable importance, not only to reduce the strain upon the blood bank, but also because blood itself carries risk of serious reactions.

Blood Volume

The individual blood capacities of the dialysing units are: Skeggs-Leonards, 550 ml.; Kolff rotating drum, 1000 ml.; Kolff twin coil, 1200 ml.; Alwall 1300 ml.

Size

The Alwall, Skeggs-Leonards and twin-coil kidneys are smaller and more mobile and, by a pressure differential between the blood and dialysing fluid circuits, effect ultrafiltration of fluid from the corporeal circulation. The Kolff rotating drum machine is much larger and relatively fixed and is not capable of ultrafiltering fluid from the overhydrated patient.

Urea Clearance

A comparison of urea clearance with different types of artificial kidneys is revealed in the following table:

Type of Artificial Kidney	Urea Clearance: Per Cent
Alwall	47.0
Kolff twin coil	56.0
Skeggs-Leonards	63.5
Kolff-rotating drum, modified (4½ hours)	75.0

(After Edwards, 1963[10] Modified)

Biochemical Adjustment

Urea clearance is not the only requirement for a successful dialysis as there must also be a satisfactory biochemical adjustment in the plasma composition: (1) reduction of the plasma K concentration where hyperkalemia exists to values within the normal range and preferably to approximately 3.5 to 4 mEq./L., (2) stabilization of the plasma bicarbonate levels at approximately 20 mEq./L. where the initial values are materially lower, (3) adjustment of Na, Cl and Ca to approximately low normal values. Higher levels of Na should not be sought because of the possible encouragement of water retention.

When comparing these machines, it must be remembered that a team knowledgeable in the management of these types of patients is of more importance than the type of machine used.

Mechanism

Most artificial kidneys are constructed in such a manner that the patient's blood is dialyzed against a physiological salt solution with cellophane acting as the semipermeable membrane. Waste products of metabolism such as urea and creatinine move through the pores of the membrane from a place of high concentration, the blood, to one of low concentration, the dialysate. Larger particles such as proteins, blood cells and bacteria cannot pass through the membrane.

The Kolff twin-coil disposable kidney is presently being used at Mt. Sinai Hospital. A schematic illustration of its function is shown in Figure 3.

If general anticoagulation of the patient leads to danger of hemorrhage, regional anticoagulation is used. Heparin is administered to the blood flowing from the patient to the artificial kidney and a neutralizing dose of protamine sulfate is administered simultaneously to the blood flowing from the artificial kidney back to the patient.

Continued

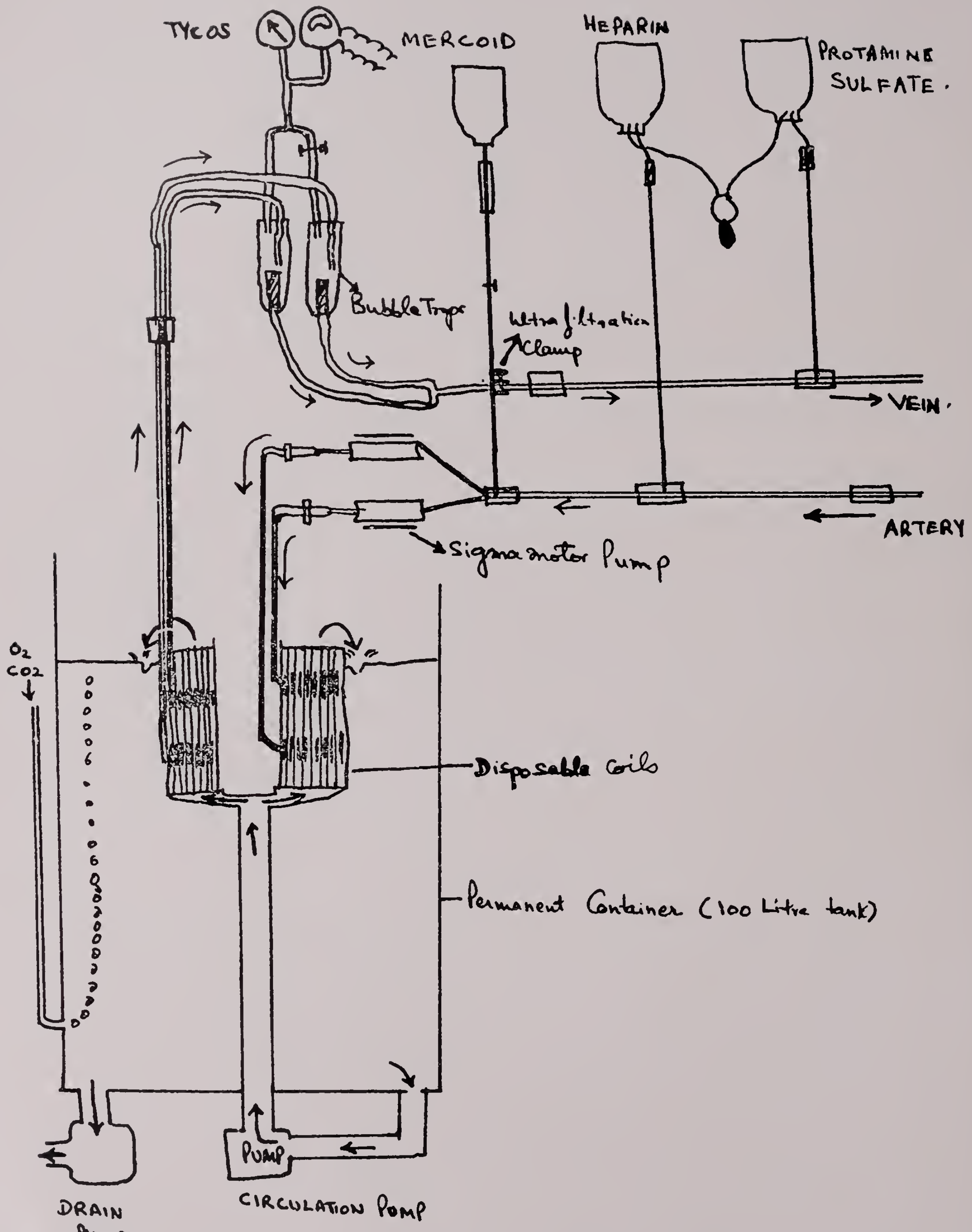
TYCOS
MERCOID
HEPARIN
PROTAMINE SULFATE.
Bubble Traps
Ultrafiltration Clamp
VEIN.
ARTERY
Sigmamotor Pump
O_2
CO_2
Disposable coils
Permanent Container (100 Litre tank)
PUMP
DRAIN PUMP
CIRCULATION PUMP

Fig. 3 — Schematic, Kolff twin coil disposable kidney.

Indications

Extracorporeal hemodialysis has been successfully used in the following conditions:[12]

Acute Renal Insufficiency

1. Following peripheral circulatory collapse, e.g., profound hemorrhage, severe anoxia, acute pancreatitis, trauma, head injuries, severe dehydration, carbon monoxide intoxication, myocardial infarction, septicemia and post-partum acute renal failure resulting from abruptio placenta or severe electrolyte disturbance.[13]
2. Hemoglobinuria and myohemoglobinuria, e.g., crush syndrome, sickle-cell crisis, transurethral prostatectomy with hemolysis, incompatible blood transfusions, icterus neonatorum, hemorrhagic fever, severe burns.
3. Acute obstruction of ureters.
4. Selected cases of acute glomerulonephritis.
5. Hepatorenal syndrome and hepatic coma.
6. Acute renal failure supervening on existing renal disease.

Acute Poisoning

1. Nephrotoxic substances: heavy metals (mercury, bismuth, phosphorus, uranium); antibiotics (bacitracin, viomycin, etc.); leptospirosis; eclampsia; bacterial toxins, sulfonamides, serum sickness; organic compounds (carbon tetrachloride, black widow spider poisons, mushrooms, etc.)
2. Dialyzable Poisons:
    - Phenobarbital
    - Barbital
    - Secobarbital
    - Tolbutal
    - Amobarbital
    - Pentobarbital
    - Doriden (Glutethimide)
    - Bromide
    - Acetyl salicylate
    - Methyl salicylate
    - Dilantin
    - Strontium
    - Radio calcium
    - Tritium
    - Potassium thiocyanate
    - Ammonia
    - Sodium chlorate
    - Antifreeze
    - Ethyl alcohol
    - Methyl alcohol
    - Bichloride of mercury
    - Iron

It is obvious that the best results will be obtained in the above two groups of cases. These patients have reversible disease and need to be supported until spontaneous diuresis and recovery occurs, or until the noxious and toxic agent is removed.

Other Indications

1. Removal of edema and correction of electrolyte problems in severe congestive heart failure.
2. Long-term problems in the care of chronic renal insufficiency in selected cases of chronic uremia.
3. Investigation of the uremic syndrome as an experimental procedure in the laboratory.
4. In acute gouty arthritis, with refractory hyperuricemia.[18]

Acute renal failure is defined as "an advanced quantitative reduction in renal function to a point where the kidneys are unable to maintain chemical

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homeostasis in the organism".[14] Acute reversible renal failure may be caused by a broad spectrum of diseases that have anuria or oliguria as their characteristic.

Many patients with acute renal failure are able to survive with meticulous attention to fluid restriction, correction of electrolyte abnormalities, therapy of infection and supportive care. However, there are two groups of patients needing extracorporeal hemodialysis for survival: (1) patients with prolonged anuria, and (2) patients with marked tissue destruction. The following are some of the indications necessitating dialysis:[15]

Clinical Criteria for Dialysis

Deterioration of Clinical Status

Dulling mental acuity, confusion, restlessness, pernicious vomiting and hiccough. Convulsions and diminishing blood pressure are late features.

Laboratory Findings:

1. Blood urea nitrogen of more than 400 mg% in medical and obstetric cases or 300 mg% in surgical cases. Some authorities do not place much value on the absolute figure for blood urea, but maintain that a daily rise of blood urea of 30 mg% or more with an absolute figure of even as low as 100 mg% is an indication for dialysis if the patient's over-all clinical status warrants it.
2. Serum K of 7 mEq./L. or more.
3. CO_2 combining power of less than 13 mEq./L.

Dialysable Toxins

1. Molecular size is small enough to diffuse through cellophane (i.e., dialysable).
2. Distribution of the substance in the body is such that it is available for dialysis from plasma (i.e., not protein-bound).
3. There is a relationship between toxicity, amount ingested and the duration of body exposure.
4. Dialysis contributes heavily to the removal of the noxious substances.

Chronic Uremia

The care of patients with chronic renal insufficiency is often ineffective. The patient with a diminishing glomerular filtration rate may be supported over periods of crisis and returned to his usual status with dialysis.

In contrast to this type of patient, there is a group of patients with more advanced deterioration of renal function who will not tolerate even minor illnesses because of marked decrease in renal reserve. Scribner[17] has pioneered methods for chronic vessel cannulation and intermittent hemodialysis in patients with terminal uremia. The concept of weekly or semiweekly hemodialysis has been applied to a group of patients with rather remarkable results. However, the cost of keeping up such a procedure for any length of time is a prohibitive factor.

Group IV: Removal of Edema

Ultrafiltration is a relatively new method available for the reduction of excess body water in patients refractory to diuretics.[19]

Complications

Rosen et al.[20] describe a dialysis disequilibrium syndrome. This syndrome is more severe when the plasma urea is very high before dialysis and manifests itself when the blood chemistry improves. First evidence is increasing lassitude, headache, drowsiness and confusion. In more severe cases there is an increase in blood pressure, pulse rate and respiratory rate. This is actually a "water intoxication" resulting from the fact that urea clearance during dialysis lags behind in the cerebrospinal fluid. This "urea gradient" results in cerebral edema.[21]

Atrial fibrillation and flutter during hemodialysis and terminating shortly after cessation of the dialysis may result from right atrial distension due to the rapid flow of blood from the coil to the patient.[22] The almost immediate conversion from atrial fibrillation to regular sinus rhythm on the termination of the dialysis indicates a hemodynamic mechanical etiology rather than blood chemical alterations.

Hypotensive reactions sufficiently severe to warrant the use of pressor amines are known to occur when blood is used to prime the dialyser. Mechanisms underlying this reaction are not clear, but use of a solution of 5% human serum albumin in 0.9% NaCl for priming avoids such reactions.[23] The apparent efficacy of albumin solution in avoiding such reactions has not been explained.

Case Histories

Case No. 1

A 41-year-old white woman was admitted to Mount Sinai Hospital December 11, 1964, with a history of severe hypertension for several years and probably beginning during one of her many (10) pregnancies. She had not responded to medical management of the hypertension, and approximately eight weeks prior to admission had begun to have epigastric pain, more severe hypertension, and anemia down to 7 gm. of hemoglobin. Her blood urea nitrogen was 16 mg% in November 1964, had risen to 69 mg% by 12/2/64, and had increased further to 110 mg% at the time of her transfer to Mount Sinai Hospital on 12/11/64. Ten days before admission she had had a hypertensive crisis with convulsions. Extensive investigation including GI X rays during November 1964, failed to reveal any other basis for the anemia. A bone-marrow examination revealed erythroid hyperplasia. Treatment with several antihypertensive drugs failed to lower her blood pressure. Serum K had risen to 6.6 Meq/L a week before admission.

Examination on admission revealed blood pressure of 210/120 in both arms. The patient was confused and lethargic. There was no dyspnea or orthopnea. Fundi showed arteriolar narrowing, AV nicking, and many small hemorrhages and exudates. There was no papilledema. There were bilateral basal pulmonic rales. Heart tones were clear with a sinus rhythm of 80/min. There was widely split second heart sound at the apex and base. The heart was markedly enlarged to the left, and there was a leathery systolic squeak consistent with a pericardial friction rub. The liver was enlarged 6 cm. below the costal margin. There was no splenomegaly. The abdomen was otherwise negative. There was no peripheral edema. The tongue was somewhat dry and there was no evidence of overhydration. On admission she had 8.3 gm% hemoglobin, normal total and differential white blood count, 2+ albuminuria, blood urea nitrogen 117 mg%, serum Na 112 Meq/L, K 3.2 Meq/L, serum creatinine 13 mg%, uric acid 15.3 mg%, CO_2 content of 23 Meq/L, chlorides 69 Meq/L, serum Ca 7.3 mg%, P 10.7 mg% and a normal liver profile. A 24-hour urine (950 ml.) had a total of 8.7 Meq Na, 21 Meq K, 1.8 Meq chloride. She was put on tetracycline and later on chloromycetin to control a urinary tract infection due to E. coli.

She was treated with large doses of guanethidine, restricted fluid intake, 1000 - 1500 ml/day, and hypertonic saline. Retrograde pyelogram revealed no evidence of obstruction. By 12/15/64 it was apparent that she was clinically deteriorating. She was "run" on the artificial kidney for six hours the same day. Before the dialysis blood urea nitrogen was 123 mg%, uric acid 13.7 mg%, CO_2 content 22 Meq/L, chloride 81 Meq/L, Na 121 Meq/L, K 4.8 Meq/L, Calcium 8.1 mg% and P 6.4 mg%. Following the

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dialysis, blood urea nitrogen was 59 mg%, creatinine 6.2 mg%, uric acid 6.8 mg%, CO_2 content 26 Meq/L, chlorides 92 Meq/L, Na 133 Meq/L, K 3.7 Meq/L, Ca 10 mg% and P 6.5 mg%.

After dialysis, as much as 200 mg. guanethidine, 425 mg. Apresoline, in addition to 10 mg. reserpine daily failed to bring her blood pressure down. By 12/17/64 she was anuric with blood urea nitrogen rising. Because of her failure to respond it was felt that she had terminal and irreversible renal failure, and it was decided not to dialyse again. The family elected to take her back to the local hospital. Renal biopsy was not attempted because of the extreme hypertension.

The patient expired two days after return to the local hospital. Autopsy revealed findings consistent with malignant (accelerated) nephrosclerosis. Her blood urea nitrogen before death rose to 172 mg%, and she remained oliguric.

Case No. 2

This 57-year-old white man, who was admitted to Mount Sinai Hospital January 22, 1965, had had a myocardial infarction three years before and had suffered from recurrent congestive heart failure for two years. He had been reasonably well controlled with salt restriction and intermittent diuretics. He had had no digitalis since May 1964. For 10 days before admission he had had marked oliguria, increasing edema, lethargy and dyspnea. On 1/20/64 he was admitted to another hospital and for the next 48 hours his total urinary output was 93 ml. He was then transferred to Mount Sinai Hospital for hemodialysis.

Examination on admission revealed blood pressure 110/70 in both arms, respiratory rate 26/min., and apical rate 88/min., regular. The fundi showed moderate arteriosclerotic change. Neck veins were distended; the abdomen was tense with ascitic fluid, and there was edema extending up to the thighs. There were crepitant rales at both lung bases and the heart was markedly enlarged.

On admission, blood urea nitrogen was 126 mg%, CO_2 content 17 Meq/L, chlorides 101 Meq/L, Na 138 Meq/L, K 5.7 Meq/L. A small amount of urine was obtained and revealed 1+ albumin. Electrocardiogram showed changes consistent with left ventricular strain. Chest revealed marked cardiac enlargement and pulmonary congestion.

Within four hours after admission, the patient was put on the artificial kidney and had a uneventful six-hour run. The artificial kidney blood outflow was partially clamped during the run to produce ultrafiltration and removal of body water. At the end of the dialysis he had lost 10 lbs. in body weight (from 151 lbs. down to 141 lbs.). Blood urea nitrogen was 82 Meq/L, Co_2 content 23 Meq/L, Cl 97 Meq/L, Na 137 Meq/L, and K 4.8 Meq/L. During the 24-hour period following dialysis his urinary output was 2980 ml. with specific gravity of 1.007 - 1.010. During the five days after dialysis he had had a urinary output averaging 3000 ml. per 24 hours and his weight had decreased and stabilized at 126 lbs. He had lost a total of 25 lbs. in this five-day period, and his ascites and peripheral edema had disappeared. Blood urea nitrogen had risen to 126% by the second day post dialysis but fell to 60 mg% by the sixth day. He was alert and no longer dyspneic. He was kept in negative water balance until the fourth post-dialysis day, at which time fluid replacement was kept equal to losses. Serum electrolytes have been maintained at normal levels without difficulty.

This patient probably represents a case of arteriosclerotic heart and kidney disease with superimposed severe and acute congestive heart failure associated with further renal decompensation and anuria. He was moribund on admission. Hemodialysis appears to have reversed his progressing heart and renal failure and at least temporarily returned him to his previous stable state.

Surendra Sethi, M.D.
Resident, Mount Sinai Hospital

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6-23 May be obtained from the Grand Rounds Editor.

Abstracts, Briefs and Commentaries

THE FATE OF DACRON VASCULAR GRAFTS

The authors present their data on 67 Dacron grafts removed in a period of from one to seven years in 58 patients. The grafts were removed for a variety of reasons (aneurysmal formation at the site of anastomosis and death of the patient from other causes). The important laboratory studies included electron microscopy as well as conventional histologic studies of the specimens.

The characteristic microscopic feature was the formation of two distinct layers, an inner and outer cellular membrane, surrounding the Dacron prosthesis and well incorporated by fibrous tissue into the Dacron interstices. There was only rare endothelialization on the inner surface of the graft beyond the immediate area of the anastomosis. The majority of the inner portions of the graft were lined by fibrous tissue. There was one degeneration by lipoid material but no evidence of calcification in the inner layer.

The authors then compared the fate of prosthetic graft in man to that of the graft in animals. In general the grafts in man fared better, in that the inner lining remained thin, did not proliferate unduly and did not occlude the graft, as so often happened in the pig. In man, the grafts performed well in various locations in the abdominal aorta and extending into the region of the popliteal artery.

The authors presented their procedures with multiple pictures and diagrams. It is interesting to note that they would operate again on the patients who developed aneurysmal formations or occlusions beyond the site of the original graft. A most impressive fact is that the prosthetic vascular grafts functioned well in the absence of an endothelial lining and there was no report of a slough of the false lining with secondary occlusion of the graft. My own experience with Dacron grafts indicates that this is an excellent substitute at least in the interabdominal vessels. The use of the synthetic prostheses in bypasses of the femoral and popliteal arteries is not as yet clarified in my mind, and vein grafts are still preferred.

Jerome Grismer, M.D.
Minneapolis, Minnesota

DeBakey, M. E., Jordan, G. L., Abbott, J. P., Halbert, B., and O'Neill, R. M.: The Fate of Dacron Vascular Grafts. Arch Surg 89:757, 1964.

CANCER OF THE BREAST IN OLD AGE

Haagensen and associates have studied a series of 556 consecutive radical mastectomies of all ages. They used the Columbia clinical classification in which Stage A reveals no clinically axillary adenopathy. Stage B reveals lymph nodes less than 2.5 cm. Stages C and D are more advanced.

They found that the results indicate a better prognosis in the older age group (over 65) than in the younger group. They also found that the operative mortality was not increased and there was no operative death in the older age group. It was their opinion that advanced cardiovascular disease, diabetes or old age was not a contraindication to radical mastectomy, and they came to the logical conclusion that radical mastectomy is the treatment of choice for operable mammary carcinoma in women, even in the aged.

The five and ten-year survival rate in the group of aged patients, after elimination of those dying of intercurrent disease, was 78.5 and 55.2 per cent, respectively. The survival rate in the younger group was less than that.

One occasionally hears it said that a patient is too old to tolerate a radical mastectomy. This study of Haagensen et al. clearly points out the futility of taking such a pessimistic attitude toward women who have attained their 65th birthday. Indeed, it is probably true that very few 65-year-old women consider themselves to be aged.

Simple mastectomy has almost no place in the armamentarium of a trained surgeon.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Papandrianos, E., M.D., Cooley, Edith, Ph.D., and Haagensen, C.D., M.D.: Mammary Carcinoma in Old Age. Ann Surg 161:189, 1965.

AMELOBLASTOMA

The clinical course and the follow-up study of 33 patients with ameloblastoma are reported. The tumor arose in the mandible of 27 patients, and in the maxilla of six. The patients, when first seen, were classified into two groups: 14 patients who had recurrent disease, and 19 who were not previously treated. Of the 14 patients who had recurrent disease, all had had initial local excision of the tumor; four had had another local procedure, all of whom had recurrence. Of the patients who had wide resection of the tumor and the jaw, seven were cured, and two were lost to follow-up. One died of distant metastases. Of the 19 patients with previously untreated ameloblastoma, 14 had had local removal of the tumor, and eight had recurrences. Only four remained free of tumor. Three had wide excision of the tumor and adjacent bone, and all remained free of tumor. Two were lost to follow-up. Because ameloblastoma of the jaw can recur locally, and can extend widely and cause death, an adequate resection of the tumor and jaw is recommended as the treatment of choice.

Courtesy of References and Reviews
Journal of the American Medical Association

Goldwyn, R., Constable, J., and Murray, J.: New Engl J Med 269:126, 1963

VAGINAL EXAMS DURING LABOR

A bacteriologic study of vaginal examinations in labor was made at the Santa Clara County Hospital on about 1000 women, about half of whom had vaginal examinations while the others had rectal examinations. On admission to the maternity ward every patient's vulva was scrubbed with soap and water and then shaved. Vaginal examinations were performed in half the labor rooms and rectal examinations in the other half; the women were assigned to one or the other group alternately.

Old rubber gloves were worn for both vaginal and rectal examinations; they were autoclaved and kept in sterile canisters, but no further effort was made to keep them sterile. Before vaginal examination 1:4000 aqueous benzalkonium chloride was poured over the vulva. Only in cases of gross contamination was this repeated.

The examiners did not scrub their hands before putting on the gloves, but when it was desirable to do a vaginal examination on a patient from the rectal group she was taken to the delivery room and fully prepared and draped, and the examiners then scrubbed their hands for three minutes with hexachlorophene soap.

The patients were routinely discharged on the fourth post partum day unless they were febrile; if they had fever they remained in hospital until their temperature had been under 100.4° F for at least 24 hours.

For the bacteriologic examination each patient on the third post partum day was placed on an examination table; a sterile speculum was inserted into the vagina; the cervix was visualized and a specimen was taken from the endocervical canal, with care that it was not contaminated by vaginal discharge.

Little difference was found between the two groups in factors that might influence morbidity. Statistically the vaginal group had a somewhat longer period between rupture of the membranes and delivery, and slightly more examinations than the rectal group.

Among the 543 patients examined vaginally there were 18 cases of morbidity according to the standard adopted; five of these had marked breast engorgement with severe tenderness, one had pharyngitis and another had severe contact dermatitis. Urinalysis in all cases was negative and there was no clinical evidence of endometritis. Among the 514 patients examined rectally during labor there were 13 cases of morbidity, one probably due to breast engorgement.

In the vaginal group a streptococcus was cultured in 11 of 17 cases and *Escherichia coli* was cultured in one. In the rectal group *E. coli* was cultured in eight of 12 cases and a streptococcus was found in one. Evidently seeding from the fecal area was the greater when rectal examinations were done. No statistical difference was found in the morbidity of the two groups.

There seemed to be no need for more extensive preparation of patient for a "sterile" vaginal examination. The simple procedure outlined here appeared to be as safe as rectal examination, and the results may help to dispel the deep-seated fear of doing vaginal examinations on patients in labor.

Courtesy of World Wide Abstracts

Bertelsen, Horace, Johnson, Bert: Amer J Obstet Gynec 85:4,527.

INFECTIOUS MONONUCLEOSIS

Twenty-six of the 100 cases of infectious mononucleosis treated in a Naval Hospital between March, 1961, and May, 1962, were included in a double-blind study of the treatment of this disease. They included a placebo-treated group of five cases; aspirin-treated, eight cases; chloroquine-treated, five cases; and prednisone-treated, eight cases.

From analysis of the fever, signs and symptoms and the duration of illness, total hospital stay and stay in hospital after treatment, it was concluded that none of the drugs, with the possible exception of intravenous steroids (which were administered to two patients because of airway obstruction from pharyngeal edema), were beneficial to the basic disease.

The best treatment for infectious mononucleosis is symptomatic. Some patients obviously have secondary invaders in the tonsils and pharynx. The pathogens detected in this series were varied and mostly incidental. This complication is best treated with the appropriate antibiotics as determined by culture.

Jaundice, the usual manifestation of hepatic complications, was present in nine cases. It is best treated with rest in bed and a high-calorie diet.

Only one case of splenic rupture has been seen at this hospital among more than 500 cases of infectious mononucleosis in the last seven years. This followed over-vigorous palpation of the spleen. It is recommended that only one person should palpate the spleen and he should do it gently and not more than twice a week.

Courtesy of World Wide Abstracts

Schumacher, Harold: Ann Intern Med 58:2,217.

PROTEIN ABNORMALITIES IN ULCERATIVE COLITIS

An antinuclear factor, which has been found in lupus erythematosus patients and their families, has also been found in ulcerative colitis. The sera of 98 subjects from 34 families with ulcerative colitis were examined for the presence of antinuclear and rheumatoid factors, thyroid antibodies, and positive lupus erythematosus (LE) latex tests. These were compared with a contratest group of relatives of gastric cancer patients. The antinuclear factor was found in 23% of the ulcerative colitis families, but in only 3% of the contratest group. The incidence of rheumatoid factor, thyroid antibody, and LE latex was the same in both groups.

Courtesy of References and Reviews
Journal of the American Medical Association

Thayer, W. and Spiro, H.: Gastroenterology 44:444, 1963.

MALLORY-WEISS SYNDROME

Hemorrhage from gastroesophageal lacerations caused by vomiting is known as the Mallory-Weiss syndrome. A review of the literature is presented and three new cases are reported. These lacerations may follow any event that brings about a marked increase in intra-abdominal pressure, such as vomiting, coughing, straining at stool, blunt external trauma, etc. It appears that this syndrome is frequently unrecognized in many patients with self-limited gastrointestinal bleeding. Only those cases requiring surgery or endoscopy have been recognized to date and reported as "rare" examples of Mallory-Weiss syndrome. This syndrome should be looked for in any patient with upper gastrointestinal bleeding and a history of vomiting or straining before bleeding.

Courtesy of References and Reviews
Journal of the American Medical Association

Dobbins, W.: Gastroenterology 44:689, 1963.

SWIMMER'S ITCH

Swimmers often develop skin lesions, usually with considerable pruritus, caused by *Trichobilharzia ocellata;* at the second larval stage of this organism it penetrates the epidermis and the lesions result. The condition is called swimmer's itch.

The eruptions start on the lower legs and extend upward as far as the abdomen, rarely further. Erythematous macules 2 to 200 mm. in diameter appear a few hours after the swimmer has left the water. They are pink or red with a small purple center. In 10 or 15 days the lesions gradually clear up, leaving no trace of pigmentation.

The trematode infests the digestive tracts of wild and domestic ducks and probably of other aquatic birds as well. The larvae which penetrate human skin are *Cercaria elvae.*

The condition is mild and transitory, so that therapy is hardly indicated. Washing with hot acidulated water, and bland powders or lotions have been helpful, also local applications of camphorated or mentholated oils, which might be of use prophylactically.

Courtesy of World Wide Abstracts

Bizot, M.: Concours Med 85:17, 2705.

DIGITAL ISCHEMIA

Repeated trauma to the hand may result in severe ischemia of the digits. In the heavily industrialized area of Detroit, eight personal cases were seen in ten months, and the records by Henry Ford Hospital showed two others. Nine of these patients were skilled workers in the automobile and other industries, and eight told of repeated trauma to the dominant hand incurred at work.

In increasing order of frequency these patients complained of rest pain, Raynaud's phenomenon, paresthesia in the affected fingers, coldness and nonhealing ulcers. Two patients had no signs of ischemia; the other eight had evidence of subcutaneous infarction, cyanosis, positive Allen's test, absent radial or ulnar pulsations, ischemic petechiae and hypesthesia.

Atherosclerosis, thromboangiitis obliterans and cervical compression syndrome were excluded. None of the patients had scleroderma or other systemic illness and no source for repeated emboli could be found. For medicolegal reasons arteriograms were occasionally necessary to prove that the symptoms were caused by arterial disease.

The treatment of this disorder requires the patient's close cooperation. In cases where symptoms of Raynaud's phenomenon were the only ones, therapy was conservative, namely the avoidance of further trauma to the hand, abstinence from tobacco and the provision of adequate warmth and protection for the injured member. Occasionally phenoxybenzamine was given by mouth as adjunctive therapy.

When there was severe ischemia, particularly if ulcers were present, upper thoracic sympathectomy was done with marked benefit. The most important aspect of any treatment is the avoidance of repeated trauma to the hand.

This syndrome is not rare, and physicians should recognize its importance as an industrial disease.

Courtesy of World Wide Abstracts

Schatz, I.: New Engl J Med 268:6,281.

THE COLD-WATER TREATMENT OF BURNS

Recent studies[1,2] indicate the efficaciousness of the cold-water treatment of burns. The experimental studies done on animals reveal that the surface temperature of the skin remains elevated for a considerable period of time after the burning instrument has been removed. If no treatment is given, the effects of this prolonged period of heat cause injury to the underlying tissue and death to the cells, thereby resulting in progressive tissue destruction over a period of several days and long delay in the healing process.

In the animals that were treated with cold packs or cold immersion, the surface temperature was very promptly diminished, and this cooling of the tissues resulted in less cellular damage and consequently quicker healing of the burn.

It was also observed that the effects of the burn lasted longer if clothing objects were on the skin.

Some of the conclusions drawn from these studies indicated that the tissues are subject to longer heat exposure than the actual duration of the burn, that there is continuous degeneration of the skin and underlying tissues of the untreated animal, which continues for several weeks after thermal injury, and that even delayed treatment with cold packs should be carried out immediately or as soon after the burn as possible.

Ice-cold water should not be used except for minor burns. The cold-pack treatment consists of water at approximately 15 degrees centigrade.

Carl O. Rice, M.D.
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1. Oleigsson, O. J., M.D.: Water Cooling First Aid Treatment of Scalds and Burns. Surgery 57:391, 1965.
2. King, C., M.D. and Zimmerman, Jack M., M.D.: The Effects of Surface Cooling On Penetration in Experimental Burns. Arch Surg 90:401, 1965.

Great men are rarely isolated mountain peaks; they are the summits of ranges.
— T. W. Higginson

Great minds have purposes, others have wishes. — Washington Irving

Book Reviews

Where is human nature so weak as in the bookstore? — H. W. Beecher

INFECTIOUS DISEASES OF CHILDREN — Third Edition. Saul Krugman, M.D., Robert Ward, M.D., C. V. Mosby Co., St. Louis, 1964.

The need for this third edition within seven years of a book devoted to the common infectious diseases of children indicates that the capacity for change in the texture and course of these disease is both great and rapid. The value and efficacy of routine immunizations and the power of the sulfonamides and antibiotics in modifying disease are such common knowledge as to be taken for granted. The progressive elimination of paralytic poliomyelitis since the widespread use of the Salk killed and the Sabine live attenuated polio virus vaccines is sufficiently recent to be recognized as dramatic. The potential of the live attenuated measles virus vaccine is yet to be realized, and other live attenuated virus or killed virus vaccines are yet in the stage of development.

As important as these preventive and therapeutic methods have been in altering the course of disease, newly developed diagnostic techniques, particularly those dealing with the virus diseases, have established specific virus agents as the causative agents for new clinical syndromes. Finally, the emergence of bacteria which are resistant to many of the commonly used antibiotics is yet another factor in the rapid metamorphosis of disease.

It is a tribute to the clinical and laboratory experience of the authors and the rapid workmanship of the publisher that this book is up to the minute in its factual information and appears destined to continue as a standard reference describing the common infectious diseases of children. It will continue to be a valuable and eventually thumb-worn book for those who deal with the health of children, whether they are pediatricians or general practitioners.

The chapters "Diagnosis of Acute Exanthematous Diseases" and "Control of Communicable Diseases" are excellent and I believe would be better placed as the opening two chapters of the book than as the closing chapters, but to dispute their location would be quibbling. If this book does have any serious limitation it is not in what is included in the text, for Drs. Krugman and Ward have discussed with authority those diseases with which they have extensive personal experience. However, the elimination of such important diseases as tuberculosis, syphilis, leptospirosis, and the mycotic infections prevent this book from being a comprehensive text on infectious diseases of children. When a future edition is contemplated, it might be well for the authors to seek a third author who can write on these diseases with the same authority in which they have encompassed the majority of the infectious diseases of childhood.

This book is to be recommended as well worth the purchasing price of $15.75.

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COUNSELING IN MEDICAL GENETICS — By Sheldon Reed, Ph.D. 2nd Edition. W. B. Saunders Co., Philadelphia, 1963; 278 pages.

Sheldon Reed is the director of the Dight Institute for Human Genetics at the University of Minnesota. His book is an authoritative reference on the probability of various heritable defects in different clinical situations. As Reed points out, the time has come when physicians must be prepared with the correct answers to the questions put by prospective parents concerning the probability of transmitting various defects. The parents of an anencephalic monster would be pleased to hear that "lightning doesn't strike twice in the same spot" but not so pleased to see a repetition of the genetic disaster. The chapters are illustrated with case histories, the counseling, and the outcome. I cannot quarrel with the counseling as far as it applies to genetics. However in some of his case histories the counseling, though genetically sound practically, may be dangerous to the family. In one situation in a family of three boys, two with club feet, the father wanted more children. The counseling suggested the mother feign illness and let the father learn what it means to take care of the children! This, says Reed, "is a most educational experience, beneficial for all males who are overly eager for the women to produce and care for large families." This is a feminine weapon in the battle of the sexes and a two-edged one just as likely to incise the wielder.

Reuben Berman, M.D.
Minneapolis, Minnesota

Striking the right

NOTE

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Special Article

A
Two-Year
Study
of
Clinical
Chemistry
Determinations
in
Minnesota
Hospitals

The Effect
of
Survey Participation
and
Laboratory Consultation
Upon
Accuracy and Reliability*

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In recent years evaluation studies in many areas of laboratory work have become a "way of life." Numerous evaluations have been conducted by such organizations as the Communicable Disease Center of the U. S. Public Health Service, the American Society of Clinical Pathologists, state societies of clinical pathologists, and state societies of medical technologists. Departments of health in many states, including Minnesota, have conducted such studies on a short-term or continuing basis.[1,2,3,4,5] The primary emphasis of these surveys has been placed upon accuracy and/or precision of performance in the particular laboratory area.

The major purpose of the present study was to investigate the effectiveness of technical consultation — brief but intensive in character — as a method for improving the accuracy and reliability (i.e., precision) of results of clinical chemistry determinations. The study was initiated in June 1961 by the State Department of Health in 110 volunteer hospital laboratories throughout the state of Minnesota.

This study evolved from an earlier survey[6] conducted by the Department of Health to obtain information regarding existing laboratory personnel, facilities, and technical procedures. This basic information was deemed necessary for the planning of programs which might be effective in improving

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Continued

patient-care services through the betterment of work done by existing personnel. One of the recommendations proposed as a result of this survey was the establishment of consultation services in laboratory techniques, particularly in rural areas.

The accuracy and precision of the values reported by participants were determined over a period of 22 months in 18 separate evaluations. The results obtained from these surveys were used to examine the effects of participation in the study as a whole, as well as the effects of consultation.

Review of the Literature

Only in the past 15 to 20 years has increasing emphasis been placed on the accuracy and reliability of results obtained from clinical chemistry laboratories. A number of surveys have been conducted in an effort to evaluate the accuracy and precision of chemical determinations and all have shown a need for improvement. In 1947 Belk and Sunderman[7] showed that more than 50% of the results obtained in their survey in Pennsylvania were unsatisfactory and that gross errors were made in many cases. Shuey and Cebel[8] reported similarly unsatisfactory results in Army and Air Force Hospitals in 1949.

Snavely and Golden[9-11] conducted three surveys for the Connecticut Society of Pathologists in 1949, 1951, and 1952. Results of the first survey of 21 hospitals showed that more than one third of the results were in error. The second survey included 28 hospitals and 13 commercial laboratories and showed 46% of the results outside the allowable limits. The third survey showed 35% of the results for 34 hospitals and 17 commercial laboratories in error.

Wootton and King[12] (1953) demonstrated a large disagreement in results between 21 different English hospitals examining the same specimen. An international trial was reported by Wootton[13] in 1954, in which laboratories in several countries were requested to perform tests on samples of freeze-dried horse serum as well as an accurate dilution of it. Results indicated the laboratories could compare two solutions more precisely than they could determine the true value of the constituent.

Several states conducted continuing surveys in compliance with laws governing approval of laboratories and personnel. The results of a California survey[4] of hemoglobin determinations indicated that reports were more precise than accurate and suggested a value of 5% for acceptable limits. The State Department of Health in Maryland[5] has published the findings of its survey in its Laboratory Bulletin. These results have repeatedly shown needs for improvement.

A number of evaluation studies have been carried out in Canadian laboratories. In 1955 Tonks and Allen[14] reported data on the accuracy of glucose determinations. In the first group, 25 out of 30 determinations were within acceptable limits, but in the second group only about one half of the results were acceptable. Extreme discrepancies occurred in both groups. In another study,[15] 17 out of 28 glucose determinations were not acceptable. More recently Tonks[16] has expanded his plan of study to include 170 laboratories from across Canada. These laboratories from hospitals of 100 beds or more made a total of 3762 analyses for eight components of freeze-dried serum. Over 40% of the values obtained were unacceptable by standards which were not overly strict.

The awareness of poor performance has caused some laboratories to seek means of improving the accuracy and precision of their results. Levey and Jennings[17] were the first to introduce the concept of quality control charts to monitor the quality of work done in the clinical laboratory. Since that time the applications of various types of quality control in the laboratory have been well-documented in the literature.[15,16,18-35]

Benenson et al.,[19] Freier and Rausch,[23] MacDonald et al.,[28] and Schneider[29] have published results of their experiences with continuing quality control programs, indicating the acceptable limits which they have been able to maintain during the period of control evaluation as well as the percentage of runs out of control.

Campbell[30] discusses a program organized by the Department of Health in Alberta to train laboratory aides in small rural hospitals in procedures for determining blood glucose, urea nitrogen, bilirubin, and prothrombin time—tests most frequently requested by physicians. Effectiveness of the program was ascertained by incorporating a quality control program which was carried out by participants upon returning to their own laboratories. Results early in the first year of operation indicated that 57% of all results were unacceptable, but 12 months later this figure was reduced to 18%. The over-all figure for the year for 1131 determinations was 32% "wrong" results. Experience with the program indicated that continuous operation of the quality control plan was necessary to maintain good performance.

With the exception of these reports, there is almost no information available in the literature concerning efforts to improve laboratory performance through workshops, consultation, or in-service training. Consultations in various areas of laboratory work was given to laboratory personnel in Georgia.[36] In clinical chemistry this was limited to directions in checking colorimeters and spectrophotometers, use of College of American Pathologists standards for calibration, and techniques for blood sugar and nonprotein nitrogen determinations. Effectiveness of the consultation was not evaluated.

Materials and Methods

Over 200 hospitals in the state were invited to participate in the study. Those agreeing to participate included 106 licensed general, two government-owned, and two special hospitals. Prior to initiation of the study, approval was obtained from the following state organizations: Minnesota State Board of Health, Minnesota Society of Clinical Pathologists, Minnesota Society of Medical Technologists, and Minnesota Hospital Association. Assistance in planning was given throughout the study by a technical advisory committee appointed by the Minnesota Society of Medical Technologists.

Plan of the Study

A total of 18 surveys were carried out over a period of 22 months beginning in June 1961. The study was designed to have three phases, each of which was to be evaluated with the results from six surveys. Phase I was known as the preconsultation period and the results from the Phase I surveys were used to establish a baseline of performance for individual laboratories. Consultation visits were given to selected laboratories during Phase II. The survey results from Phase III, the postconsultation period, were used to evaluate the effectiveness of consultation in visited hospitals, and the continuing performance in other hospitals after more than one year of participation.

Participants were asked to analyze two types of specimens. Samples for hemoglobin determination were prepared from outdated human blood from a blood bank.[35,37] The plasma was removed and the red cells were washed with normal saline and lysed with Triton X-100. Reagent-grade glycerol was added to dilute the final solution of hemoglobin to the desired concentration. After thorough mixing and filtering, the hemoglobin solution was dispensed in glass vials in 3-ml. quantities and stored at −20°C. until specimens were mailed.

Samples of lyophilized human serum* obtained commercially were analyzed for glucose, calcium, chloride, urea nitrogen, total protein, uric acid, and cholesterol. Both sample preparations were found to be quite stable and well suited to survey use. Selection of the determinations was based on results of a 1959 survey[6] which indicated that these tests were performed by the greatest number of hospitals in the state. The lyophilized serum bottles were coded X-1, 2,—18 and the lysed red-cell sample bottles were coded H-1, 2,—18. Both were labeled "Minn. Dept. of Health Chemistry Evaluation Sample." No arrangements were made to have the samples handled as "blind"

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*Seven special lots of Versatol, Versatol-A, and Versatol-A Alternate were obtained from Warner-Chilcott Laboratories, Morris Plains, N. J., for the study. These materials were prepared by removing or reducing various constituents in pooled serum to a known level by selective dialysis, then adding weighed amounts of these constituents back into the pools. The materials were then freeze-dried (lyophilized in glass containers). Five ml. of distilled water were added to each vial to reconstitute the serum.

*Specimens were not distributed in December of 1961 and February, April, and June of 1962.

specimens, because reconstitution of the lyophilized sample would have presented additional problems in small hospitals.

The concentrations of constituents in the lyophilized serum samples ranged from normal to varying degrees of abnormal values with one exception. Due to the insoluble nature of cholesterol, it was not possible for the manufacturer to prepare these samples with the higher amounts of cholesterol normally found in serum. The target values supplied by the manufacturer were considered to be true values for each constituent. Three lots of serum containing concentrations of constituents within normal range were used for nine surveys. Four lots of serum containing abnormal concentrations were used for the other nine surveys. Each lot was used at least twice. Eight lots of lysed red-cell samples were prepared to contain concentrations of hemoglobin which were within normal range or abnormally low. Each of these lots was used for one, two, or three surveys. The median of values reported by participants was used as the target value for each hemoglobin survey. The Communicable Disease Center in Atlanta, Ga., served as a reference laboratory for hemoglobin determinations. Their results were nearly identical with the median values reported by participants for each survey.

With the exception of four months* during Phases I and II, specimens and report forms were mailed to participants on the third Monday of each month. Participants were requested to carry out only those determinations performed routinely in their laboratories and to return their results within three weeks after specimens were received. Replicate determinations were not requested, although many laboratories reported duplicate and sometimes triplicate results.

Monthly reports giving the target values of the constituents and the mean, median, range, and standard deviation of the reported values were prepared and sent to participants on the Friday, 26 days after the specimens were mailed. Results received after the deadline were not included in these calculations nor in the data presented here. It was felt that returning reports to participants at a specific time following each survey would help to maintain interest and participation throughout the study. Receipt of the report prior to mailing the next specimen would also allow laboratories which had reported results with large errors to do a certain amount of trouble-shooting in an attempt to correct their problems before analysis of the next specimen.

At the end of each phase, a progress report was sent to participants giving summary tables and histograms of the results. Laboratories were identified by code numbers which had been assigned at the beginning of the study. Laboratories were required to return results on at least three surveys during each phase in order to be included in the remainder of the study.

Selection of Comparison Groups

In order to give each laboratory a single value which could be used for rating purposes, average "Z" scores were determined. At the completion of Phase I, "Z" scores* were computed for each laboratory on each determination result reported. These were then averaged, regardless of the number of determinations performed or the number of surveys (out of six) reported on. The laboratories were then arranged on a scale according to increasing values of average "Z" scores. The highest performing one third of the laboratories (i.e., those with the smallest average "Z" scores) were defined as the Criterion Group — those laboratories which were reporting the most satisfactory results on the average during Phase I. The remaining laboratories were randomly assigned to either the Consultation Group (the group receiving consultation visits) or to the Control Group. The Control Group represented those laboratories which showed an average performance similar to that of the Consultation Group at the end of Phase I, but whose improvement during Phases II and III would stem from self-help only. This design, the Completely Randomized Design, ensured the lack of systematic bias in allocating the laboratories to groups.

The laboratories were asked to complete

$$*Z = \frac{\text{Participant's Value} - \text{Target Value}}{\text{Standard Deviation}}$$

questionnaires at the beginning of the study, which requested information regarding the administration, training of personnel, type of equipment and supplies used, the methodology used, and other items. The Consultation and Control Groups were found to be similar with regard to working characteristics, geographical location, and average "Z" scores.

A second questionnaire was sent to all participants at the conclusion of the study in order to determine any changes in characteristics during the 22 months. Participants were also requested to list changes in personnel, equipment, etc., on the monthly report forms.

Consultation

A consultant clinical chemist made at least three visits to each hospital laboratory in the Consultation Group during the months of May through October, 1962. Consultation consisted of reviewing those methods for determinations where large or consistent errors were found in the participant's results. Such things as technique, standardization of instruments through calibration with freshly prepared standard solutions, stability and source of reagents, calculation of results, and possible sources of error in the methods and instruments were discussed. On occasion it was necessary to demonstrate the calibration of an instrument or to supply the procedure for a more reliable method than the one in current use.

Workshops were given on five alternate Saturdays during August, September, and October, 1962. Invitations were sent to laboratory personnel in all visited hospitals. Most of the laboratories sent one or two persons to one of the workshops. Two determinations, chloride and urea nitrogen, were discussed in detail and performed by participants with supervision and aid from the consultant chemist.

Analysis of Results

With the exceptions of glucose and cholesterol, methods *per se* were not evaluated in the study. Two categories were used for reporting glucose results: True Glucose, measured by methods such as that of Nelson[38] and Somogyi,[39] and Total Reducing Substances, measured by methods such as that of Folin and Wu.[40] Target values for each category were supplied by the manufacturer.

Cholesterol results were also placed in two categories. Class A included cholesterol results obtained by the Abell[41] or the Schoenheimer and Sperry[42] methods. These extraction methods were found to give more accurate results by correcting for chromogenic interference — a possible cause of erroneous results. Class B represented all other results, i.e., those obtained by various direct methods (e.g., Pearson, Stearn, & McGavack[43]), methods used by too few laboratories to be separately evaluated, or methods found to give values covering a wide range (e.g., Bloor[44]).

The allowable errors were chosen by arbitrarily assigning percentage limits for each determination (see Table 3). These limits were arrived at through consideration of the acceptable limits used by other authors[4,5,7-11,16,23,45] and were felt to be not overly strict. These limits were used for both accuracy and precision analysis.

Accuracy was defined as the ability of a laboratory to obtain results which agreed with the true values of the constituents. As mentioned earlier, the target values supplied by the manufacturer represented the true values for purposes of this study. These target values were used to compute the acceptable limits, and accuracy was then evaluated for each group by determining the percentage of laboratory results falling within acceptable limits.

Reliability, or precision, was defined as the ability of the laboratories to obtain closely repeatable results. Since precision indicates the degree of spread of the results from the average, the *mean values* of the results reported for each constituent were used to compute acceptable limits for this analysis.

The significance of changes in performance from Phase I to Phase III was determined for each group by binomial proportion analyses with probability values being obtained from a table of the normal distribution.[46] Phase II was omitted from the analysis

Continued

of results because consultation occurred during that phase. Effectiveness of consultation was measured by computing *net change* in performance — defined as the change demonstrated by the Consultation Group, corrected for the change demonstrated by the Control Group.[47]

Tables of statistical inter-relationships were used to compare technical and environmental factors with laboratory performance at the end of the baseline period.[46,48] The effect of consultation as it relates to training of personnel was also examined by this method. The questionnaires completed by the participants provided the information needed to rate each laboratory according to training of personnel, availability of a pathologist, and hospital size as indexed by bed category and chemistry workload.

Results and Discussion

Description of the Study Population

Participation According to Hospital Size

Approximately 60% of the hospital laboratories in the state participated in the study at the outset. Table 1 shows the degree of participation according to hospital size as indexed by bed category. Of the 110 laboratories that agreed to participate, 90 completed the study. Of the 20 dropouts during the course of the study, ten occurred during the baseline period, Phase I. Seven of the remaining ten who dropped out during the rest of the study were members of the Consultation Group and three were members of the Control Group. Most of these dropouts occurred during Phase III. The fact that the Consultation Group had twice as many dropouts as the Control Group suggests a possible adverse effect of the consultation visits on continued participation of those laboratories.

The allocation of laboratories to groups is also presented in Table 1 according to hospital size. It can be seen that Criterion Group laboratories were located mainly in the larger hospitals, i.e., 25 out of 35 were in hospitals with 100 or more beds. Twenty-two out of 26 Consultation Group laboratories and 25 out of 29 Control Group laboratories were located in smaller hospitals containing fewer than 100 beds and generally situated in the rural areas of the state.

The level of participation increased with hospital size. Table 1 shows that the distribution of participating laboratories was highly representative of the laboratory population in the state as far as large laboratories were concerned. The smaller hospitals, however, were not as well represented, and a bias here, due chiefly to lack of response and partly to dropouts, is clearly indicated. Better participation from the smaller laboratories would have been desirable, since the additional information could have made the results obtained more representative of laboratory performance in hospitals of less than 50 beds. The poor response from hospitals of less than 50 beds could be attributed to increased laboratory workload caused by the

TABLE I

Participation According to Hospital Size as Indexed by Bed Category

	Bed Category					
	<25	25-49	50-99	100-249	>250	Total
Laboratories Invited	50	67	31	23	17	188
Laboratories Accepting	16	39	21	18	16	110
% Accepting	32.6	58.2	67.7	78.3	94.1	58.5
Labs CompletingStudy	10	29	18	17	16	90
% of Those Accepting That Completed the Study	62.5	74.4	85.7	94.4	100.0	81.8
Labs Completing Study According to Group Allocation:						
Criterion	0	1	9	11	14	35
Consultation	4	13	5	4	0	26
Control	6	15	4	2	2	29

survey samples. This increase would have had little impact, however, on the workload of larger laboratories.

Participation According to Phases

The number of laboratories reporting results according to determination and phase is presented in Table 2. Hemoglobin was the one determination on which all participants reported. Glucose and urea nitrogen were analyzed by most laboratories. The remaining determinations in decreasing frequency of reports were cholesterol, total protein, chloride, uric acid, and calcium. Since laboratories were requested to perform only those procedures which were normally done by them, the number of reports received on each determination seemed to reflect its popularity in hospitals throughout the state. Table 2 also shows that the response was quite uniform throughout the study for each determination. At the end of the study, 42 of the laboratories had reported on all 18 surveys before the deadline; 28 of these reported on all eight determinations, and 14 reported on seven out of the eight determinations.

Effect of Participation per se on Improvement of Laboratory Results

The target values for the various lots of lyophilized sera and hemoglobin solutions are shown in Table 3 according to the survey numbers in which they were distributed. The acceptable limits are also given for each determination. The acceptable results for each determination are presented in Tables 4-12; the unacceptable results are presented in Table 13.* The total "percent acceptable"

TABLE 2
Number of Laboratories Reporting Results by Determination and Phase

Determination	Phase	No. Laboratories Reporting (No. Specimen Reports/Phase)				Total Laboratories Reporting
		3**	4	5	6	
Glucose	I	4	6	22	56	88
	II	5	5	16	62	
	III	5	4	18	61	
Calcium	I	0	3	13	37	53
	II	2	4	6	41	
	III	0	3	6	44	
Chloride	I	3	5	16	45	69
	II	5	4	10	50	
	III	2	2	14	51	
Hemoglobin	I	4	8	22	56	90
	II	5	6	17	62	
	III	7	6	16	61	
Urea Nitrogen	I	4	6	18	55	83
	II	4	6	13	60	
	III	5	5	17	56	
Total Protein	I	2	5	20	46	73
	II	3	3	13	54	
	III	5	3	12	53	
Uric Acid	I	0	7	14	38	59
	II	3	3	12	41	
	III	3	2	8	46	
Cholesterol	I	3	7	17	50	77
	II	3	7	14	53	
	III	4	7	14	52	

**Laboratories reporting on less than 3 specimens per phase were not included in analysis of the study.

Continued

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*Unacceptable results were listed according to determination and group in two categories: the number of results falling between the acceptable limits and ±20% of the target value, and the number of results which were greater than ±20% of the target value. The latter were considered extreme results.

results in terms of accuracy and precision for Phases I and III are given for each laboratory group. Improvement is indicated by a larger percentage of acceptable results in Phase III than in Phase I, thus giving a positive value in the column "Differences in Percentages (III - I)" for a particular group. Deterioration is indicated by a negative value.

To determine whether laboratory participation in an evaluation study resulted in improved accuracy and precision, the data obtained for the Criterion and Control Groups were each examined separately. In this analysis, the Criterion Group data reflected the effect of participation upon the upper one third of the laboratories, and the Control Group data represented the lower two thirds of the laboratories. The Consultation Group was omitted, since the aim here was to assess solely the effect of participation.

Although the tables show that the numbers of laboratories vary depending on the group or determination, the statistical analysis does take sample size into account. Only for true glucose were the number of laboratories for the Consultation and Control Groups undesirably small and the results perhaps inadequately determined. This situation occurred because most of the laboratories in these groups analyzed glucose by methods for total-reducing substances.

Significant improvement in accuracy was noted for the Criterion Group for calcium ($P = .002$) and cholesterol determined by "B" methods ($P = .03$). The Control Group demonstrated significantly improved accuracy in measuring urea nitrogen ($P = .01$) and uric acid ($P = .02$). [The Criterion Group improved accuracy for true glucose, calcium, uric acid, and cholesterol "A", and showed deterioration for total-reducing substances and chloride; while the Control Group showed no change for hemoglobin and total-reducing substances and improvement for calcium, chloride, total protein, and cholesterol "B". These changes did not approach significance.]

Precision for the Criterion Group showed significant improvement in the measurement of calcium ($P = .002$) and uric acid ($P = .05$) This group also showed significant deterioration in precision for total-reducing substances ($P = .04$). Those determinations performed more precisely in Phase III than in Phase I by the Control Group included calcium ($P = .004$), chloride ($P = .02$), urea nitrogen ($P = .02$), and total protein ($P = .08$). [The Criterion Group showed no change in determining hemoglobin; improvement for true glucose, urea nitrogen, and cholesterol "A"; and deterioration for chloride, total protein, and cholesterol "B", while the Control Group improved uric acid precision but showed deterioration for total reducing substances, hemoglobin, and cholesterol "B". None of these changes were significant.]

The results for the Criterion Group showed that precision was on a level comparable to that of accuracy with two exceptions — total protein and cholesterol. The group raised the level of accuracy of the cholesterol "A" methods to a par with precision in Phase III (accuracy went from 71% to 80% while precision remained about 82%). The comparable levels were maintained in both phases of the study. The Control Group, on the other hand, showed considerable variation in levels when accuracy and precision of each determination were compared. Like the Criterion Group, the Control Group demonstrated better precision than accuracy for total protein and cholesterol. In other determinations, the Control Group measured constituents with more accuracy than precision.

Although the Control Group was able to show some significant improvement in accuracy and precision, the over-all level of performance approached that of the Criterion Group in only one instance — accuracy of determining uric acid in Phase III. For some determinations, the level of performance was decidedly poor.

The fact that precision was considerably better than accuracy for total protein determination in both groups could be because many laboratories standardize their procedures with bovine albumin solutions. If these solutions have not been assayed by the Kjeldahl procedure, their use as standards

TABLE 3
Target Values of Specimens

		Lot Numbers of Lyophilized Sera						
		1	2*	3	4*	5	*6	7*
		Survey Number When Used						
Determination	Acceptable Limits	1,5,11,14	2,15,18	3,10,17	4,13	6,12	7,8	9,16
True Glucose	±10%	84 mg%	297 mg%	84 mg%	200 mg%	85 mg%	297 mg%	200 mg%
Total-Reducing Substance	±10%	100 mg%	320 mg%	100 mg%	217 mg%	98 mg%	320 mg%	220 mg%
Calcium	±5%	10.0 mg%	12.5 mg%	9.9 mg%	7.0 mg%	10.1 mg%	12.4 mg%	7.1 mg%
Chloride	±5%	101.0 meq/L	108.7 meq/L	100.5 meq/L	90.5 meq/L	102.1 meq/L	108.9 meq/L	90.0 meq/L
Urea Nitrogen	±10%	11.9 mg%	59.4 mg%	11.9 mg%	30.1 mg%	12.1 mg%	59.4 mg%	29.9 mg%
Total Protein	±5%	7.1 g%	4.5 g%	6.9 g%	4.6 g%	7.2 g%	4.6 g%	4.5 g%
Uric Acid	±7%	3.0 mg%	6.0 mg%	3.2 mg%	8.0 mg%	3.0 mg%	5.9 mg%	8.0 mg%
Cholesterol	±10%	115 mg%	93 mg%	128 mg%	90 mg%	106 mg%	94 mg%	90 mg%

Median Values of Hemoglobin Specimens

	Survey Numbers When Used							
Acceptable Limits	1	2	3,8,10	4,6	5,9	7,13,14	11,15,17	12,16,18
±5%	10.6 g%	14.7 g%	8.7 g%	12.0 g%	15.2 g%	13.4 g%	9.1 g%	12.2 g%

*Lot numbers 2,4,6 and 7 contained abnormally high amounts of bilirubin.

TABLE 4
True Glucose

		Phase I		Phase III				
Group	No. Labs	% Acceptable	No. Acceptable No. Reports	% Acceptable	No. Acceptable No. Reports	Differences in Percentages (III-I)	Std. Error* of Difference	"P" of Difference
Accuracy								
Criterion	24	77.2	105/136	81.4	114/140	+4.2%	4.9%	.38
Consultation	3	77.8	14/18	83.3	15/18	+5.5%	13.2%	.67
Control	5	75.0	21/28	82.8	24/29	+7.8%	10.8%	.47
Net-Change** (Consultation-Control)						−2.3%	17.0%	.90
Precision								
Criterion	24	77.9	106/136	82.9	116/140	+5.0%	4.8%	.80
Consultation	3	88.9	16/18	72.2	13/18	−16.7%	12.9%	.20
Control	5	64.3	18/28	86.2	25/29	+21.9%	11.1%	.05
Net Change** (Consultation-Control)						−38.6%	17.0%	.02

*See ref. 46.
**See ref. 47.

Continued

TABLE 5
Total-Reducing Substances

Accuracy

		Phase I		Phase III		Differences in	Std. Error*	"P"
Group	No. Labs	% Acceptable	No. Acceptable No. Reports	% Acceptable	No. Acceptable No. Reports	Percentages (III-I)	of Difference	of Difference
Criterion	9	94.1	48/51	86.3	44/51	−7.8%	5.8%	.18
Consultation	23	82.0	100/122	82.5	104/126	+0.5%	4.8%	.91
Control	23	79.0	94/119	78.4	91/116	−0.6%	5.4%	.80
Net Change** (Consultation-Control)						+1.1%	7.2%	.91
Precision								
Criterion	9	96.1	49/51	84.3	43/51	−11.8%	5.8%	.04
Consultation	23	83.6	102/122	86.5	109/126	+2.9%	4.5%	.52
Control	23	81.5	97/119	79.3	92/116	−2.2%	5.2%	.68
Net Change** (Consultation-Control)						+5.1%	6.9%	.46

TABLE 6
Calcium

Accuracy

		Phase I		Phase III		Differences in	Std. Error*	"P"
Group	No. Labs	% Acceptable	No. Acceptable No. Reports	% Acceptable	No. Acceptable No. Reports	Percentages (III-I)	of Difference	of Difference
Criterion	29	61.8	102/165	77.7	129/166	+15.9%	5.0%	.002
Consultation	12	47.1	32/68	47.1	33/70	0%	8.5%	.0
Control	12	43.9	29/66	57.1	40/70	+13.2%	8.5%	.12
Net Change** (Consultation-Control)						−13.2%	12.0%	.28
Precision								
Criterion	29	62.4	103/165	78.3	130/166	+15.9%	4.9%	.002
Consultation	12	45.6	31/68	42.9	30/70	−2.7%	8.4%	.75
Control	12	30.3	20/66	54.3	38/70	+24.0%	8.2%	.004
Net Change** (Consultation-Control)						−26.7%	11.8%	.02

TABLE 7
Chloride

Accuracy

		Phase I		Phase III		Differences in	Std. Error*	"P"
Group	No. Labs	% Acceptable	No. Acceptable No. Reports	% Acceptable	No. Acceptable No. Reports	Percentages (III-I)	of Difference	of Difference
Criterion	33	92.1	174/189	89.5	170/190	−2.6%	3.0%	.38
Consultation	17	54.4	50/92	70.5	67/95	+16.1%	7.0%	.02
Control	19	56.0	56/100	66.7	70/105	+10.7%	6.8%	.11
Net Change** (Consultation-Control)						+5.4%	9.7%	.58
Precision								
Criterion	33	92.6	175/189	89.5	170/190	−3.1%	2.9%	.29
Consultation	17	51.1	47/92	72.6	69/95	+21.5%	6.9%	.002
Control	19	32.0	32/100	47.6	50/105	+15.6%	6.7%	.02
Net Change** (Consultation-Control)						+5.9%	9.6%	.54

*See ref. 46.
**See ref. 47.

TABLE 8
Hemoglobin

Accuracy

Group	No. Labs	Phase I		Phase III		Differences in Percentages (III-I)	Std. Error* of Difference	"P" of Difference
		% Acceptable	No. Acceptable No. Reports	% Acceptable	No. Acceptable No. Reports			
Criterion	35	88.3	173/196	90.9	180/198	+2.6%	3.1%	.39
Consultation	26	72.7	101/139	87.5	126/144	+14.8%	4.7%	.002
Control	29	76.1	118/155	75.8	113/149	−0.3%	4.9%	.96
Net Change** (Consultation-Control)						+15.1%	6.8%	.02

Precision

Group	No. Labs	Phase I % Acceptable	Phase I No. Acceptable No. Reports	Phase III % Acceptable	Phase III No. Acceptable No. Reports	Differences in Percentages (III-I)	Std. Error* of Difference	"P" of Difference
Criterion	35	88.8	174/196	88.4	175/198	−0.4%	3.2%	.90
Consultation	26	73.4	102/139	85.4	123/144	+12.0%	4.8%	.01
Control	29	78.1	121/155	73.2	109/149	−4.9%	4.9%	.32
Net Change** (Consultation-Control)						+16.9%	4.7%	.01

TABLE 9
Urea Nitrogen

Accuracy

Group	No. Labs	Phase I		Phase III		Differences in Percentages (III-I)	Std. Error* of Difference	"P" of Difference
		% Acceptable	No. Acceptable No. Reports	% Acceptable	No. Acceptable No. Reports			
Criterion	32	63.9	117/183	70.3	130/185	+6.4%	4.9%	.20
Consultation	23	24.8	31/125	45.7	59/129	+20.1%	5.9%	.001
Control	28	33.1	49/148	47.2	67/142	+14.1%	5.7%	.01
Net Change** (Consultation-Control)						+6.0%	8.2%	.46

Precision

Group	No. Labs	Phase I % Acceptable	Phase I No. Acceptable No. Reports	Phase III % Acceptable	Phase III No. Acceptable No. Reports	Differences in Percentages (III-I)	Std. Error* of Difference	"P" of Difference
Criterion	32	65.6	120/183	73.0	135/185	+7.4%	4.8%	.12
Consultation	23	34.4	43/125	49.6	64/129	+15.2%	6.1%	.01
Control	28	25.7	38/148	38.0	54/142	+12.3%	5.4%	.02
Net Change** (Consultation-Control)						+2.9%	8.2%	.73

TABLE 10
Total Protein

Accuracy

Group	No. Labs	Phase I		Phase III		Differences in Percentages (III-I)	Std. Error* of Difference	"P" of Difference
		% Acceptable	No. Acceptable No. Reports	% Acceptable	No. Acceptable No. Reports			
Criterion	32	42.9	78/182	48.6	90/185	+5.7%	5.2%	.27
Consultation	19	21.7	23/106	31.1	33/106	+9.4%	6.0%	.12
Control	22	25.4	29/114	30.7	35/114	+5.3%	5.9%	.38
Net Change** (Consultation-Control)						+4.1%	8.4%	.62

Precision

Group	No. Labs	Phase I % Acceptable	Phase I No. Acceptable No. Reports	Phase III % Acceptable	Phase III No. Acceptable No. Reports	Differences in Percentages (III-I)	Std. Error* of Difference	"P" of Difference
Criterion	32	75.3	137/182	71.9	133/185	−3.4%	4.6%	.46
Consultation	19	41.5	44/106	50.9	54/106	+9.4%	6.8%	.16
Control	22	34.2	39/114	45.6	52/114	+11.4%	6.4%	.08
Net Change** (Consultation-Control)						−2.0%	9.4%	.84

*See ref. 46.
**See ref. 47.

Continued

tends to over-estimate the true value of the protein content in the sample. Some variation in protein content as determined by the Kjeldahl procedure will also occur, depending on the type of catalyst used.*

The large difference in the numbers of acceptable results for the two classes of cholesterol methods is noteworthy. The "B" methods as a whole fall considerably short of the "A" methods in terms of both accuracy and reliability. The more time-consuming extraction procedures of Abell[11] or Schoenheimer and Sperry[12] consequently result in a high degree of accuracy and a comparable level of precision. As mentioned earlier, the "B" methods include so-called direct methods which have been shown to be adversely affected by high concentrations of serum bilirubin which in turn cause the cholesterol values to be falsely high, usually in a proportionate manner.

Effects of Consultation on Improvement of Laboratory Results

In the preceding section, the results obtained for the Criterion and Control Groups were derived from participation alone. Similarly the Consultation Group data stemmed from participation, but on the other hand, were also affected by the consultation visits given during Phase II. The *gross changes* (i.e., Phase III–Phase I differences in percentages) in accuracy and precision included both participation and consultation effects, while *net changes* measured the effect of consultation only. As defined earlier, net change was the change from Phase I to Phase III shown by the Consultation Group, corrected for the change shown by the Control Group. If the Consultation Group showed significant improvement over and above that of the Control Group, this could be interpreted as a net improvement due to consultation.

Grossly, the Consultation Group demonstrated significant improvement in accuracy for chloride ($P = .02$), hemoglobin ($P = .002$), urea nitrogen ($P = .001$), and cholesterol "B" ($P = .003$). Precision showed significant improvement for chloride ($P = .002$), urea nitrogen ($P = .01$), and hemoglobin ($P = .01$). [In terms of accuracy, the group showed no change in total-reducing substances and calcium and slight improvement in total protein and uric acid, while precision improved somewhat for total-reducing substances, total protein, uric acid, and cholesterol "B" and deteriorated for calcium. None of these changes were significant.]

Turning now to the question of consultation, it can be seen that intensive consultation was shown to be effective for only one determination. A significant net change was demonstrated for hemoglobin, since the Consultation Group showed marked improvement in both accuracy and precision and the Control Group did not. It is possible that the effect was thus seen for hemoglobin because this determination was the simplest to perform of all those included in the study. Therefore, corrections in methodology and technique were neither difficult for the consultant chemist to suggest nor for the laboratorian to comprehend.

The only other significant net change was that for calcium, namely, a net deterioration in precision. The explanation is not at hand; it is possible that this was related to the fact that the calcium determination was not emphasized as much as certain other determinations during the consultation visits.

Comments

When the study was initiated, it was hoped that the consultation would be given as intensively as possible and that each consultation laboratory would receive about one visit per month during the six-month consultation period. Due to a shortage of personnel during Phase II, each visited laboratory received only three visits. This may have contributed to the lack of sufficient evidence to support the premise that intensive consultation has a measurable beneficial effect.

Since the consultation and control laboratories were selected randomly from the lower-performing two thirds of the study sample, the two groups should have differed from each other only by chance, for each determination during Phase I. The tables show some differences between the two groups for Phase I, and these differences were significant for precision of measuring calcium, chloride, uric acid, and cholesterol. In retrospect, other factors (e.g., training of personnel, dropouts, turnover of personnel, hospital size) come to mind, which could have caused these differences but which were not apparent at that time. These findings suggest that a better design for selection of laboratory groups could have been employed which would have controlled some of the random variables more closely. Examples of such designs are the Matched Pair design and the Randomized Block design. While comparison of the two groups following randomization showed that they were similar in qualitative ways, one of these designs would have provided for a quantitative balancing of the two groups.

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*Laboratories which do not have facilities for performing Kjeldahl analyses may be interested in knowing that standard protein solutions are available from the College of American Pathologists.

Awareness of a problem of nonscientific nature also occurred during the study. When a person associated with a state agency attempts to aid laboratories in improving their work, the efforts of the consultant take on the aura of a "policing" action. This effect can be overcome only by the establishment of good rapport between participant and consultant. Although this is not always an easy situation to establish, the absence of good rapport would most probably result in total ineffectiveness of consultation.

Relationship of Laboratory Results to Some Technical and Hospital Factors

One of the singularly important items which can be gleaned from the literature concerning laboratory evaluations is the consensus of opinion regarding the cause of poor performance. Most authors attribute inaccurate results to inadequately trained or inexperienced personnel, to lack of adequate supervision, and to the pressures of excessive workloads.[3,7,8,9,11,15] An attempt was made, therefore, to utilize the data obtained from individual laboratories for comparison of over-all performance with the following three factors: training of personnel, availability of a pathologist, and hospital size. The latter was indexed by two related variables — chemistry workload and bed category.

Information given on questionnaires completed by the participants was used to classify each of the ninety laboratories with respect to these four items, employing only results from the baseline period, Phase I, for the analysis. Data were pooled for each laboratory, regardless of determinations, to give a ratio score for accuracy and for precision of the total number of acceptable results over the total number of reports received.

Training of Personnel

Laboratories were classified according to the level of training of their personnel. If

TABLE 11
Uric Acid

		Phase I		Phase III				
Group	No. Labs	% Acceptable	No. Acceptable No. Reports	% Acceptable	No. Acceptable No. Reports	Differences in Percentages (III-I)	Std. Error* of Difference	"P" of Difference
Accuracy								
Criterion	30	55.6	95/171	58.1	100/172	+2.5%	5.4%	.63
Consultation	13	36.2	25/69	46.6	34/73	+10.4%	8.2%	.21
Control	16	41.9	36/86	59.3	51/86	+17.4%	7.5%	.02
Net Change** (Consultation-Control)						−7.0%	11.1%	.52
Precision								
Criterion	30	57.9	99/171	68.0	117/172	+10.1%	5.2%	.05
Consultation	13	21.7	15/69	28.8	21/73	+7.1%	7.3%	.33
Control	16	36.0	31/86	43.0	37/86	+7.0%	7.4%	.37
Net Change** (Consultation-Control)						+0.1%	10.4%	.99

*See ref. 46.
**See ref. 47.

Continued

one or more persons in the laboratory were registered by the American Society of Clinical Pathologists with or without a degree, were California state-licensed with or without a degree, or had a baccalaureate degree or higher from an accredited college in a scientific field, they were classified as "American Society of Clinical Pathologists registered or equivalent (ASCP)." Laboratories were classified as "Other" if their personnel had received their training from a commercial trade school, a laboratory assistant program, the Armed Forces, or on-the-job. The results for the two classifications in terms of accuracy and precision are given in Table 14, part 1a. The results clearly indicate that the ability to perform laboratory tests accurately and reliably is related to the level of training of the personnel. The differences between the performance of the well-trained personnel and that of the less-well-trained personnel were significant for both accuracy and precision ($P = << .001$ in each case).[46]

The results for the Consultation and Control Groups were also examined with respect to the level of training of personnel. The scores for individual laboratories in both groups for Phases I and III were used for this analysis. (See Table 14, part 1b.) The improvement seen in both groups for "American Society of Clinical Pathologists (ASCP)" was significant for both accuracy and precision ($P = .01$). The improved accuracy and precision for "Others" in the Consultation Group were significant ($P = .02$), while the changes for "Others" in the Control Group were not.

These results imply that well-trained personnel are capable of improving laboratory performance through participation in evaluation studies alone. On the other hand, participation alone apparently does not provide any benefit for less-well-trained personnel. Consultation appears to have a real effect in upgrading the level of performance of the less-well-trained people. Whether the newly attained level can be maintained without continued consultatory aid, particularly when turnover occurs, is quite doubtful.

Availability of a Pathologist

Laboratories were classified according to three categories for this analysis: "Yes" if the laboratory had the services of a resident pathologist or received daily visits from a pathologist, "Occasional" if the laboratory received periodic visits from a pathologist, and "No" if no pathologist visited the laboratory at any time. The results are given in Table 14, part 2. The differences among the three categories were significant for both

TABLE 12
Cholesterol

Group	No. Labs		Phase I		Phase III		Differences in Percentages (III-I)	Std. Error* of Difference	"P" of Difference
			% Acceptable	No. Acceptable No. Reports	% Acceptable	No. Acceptable No. Reports			
Accuracy									
Criterion	12	A Methods	70.8	46/65	80.0	56/70	+9.2%	7.4%	.24
	18	B Methods	26.7	28/105	40.4	42/104	+13.7%	6.5%	.03
Consultation	20	B Methods	15.3	17/111	32.1	35/109	+16.8%	5.6%	.003
Control	24		18.8	24/128	24.4	30/123	+5.6%	5.2%	.28
Net Change** (Consultation-Control)							+11.2%	7.6%	.14
Precision									
Criterion	12	A Methods	81.5	53/65	82.9	58/70	+1.4%	6.6%	.84
	18	B Methods	58.1	61/105	53.8	56/104	—4.3%	6.9%	.54
Consultation	20	B Methods	47.8	53/111	49.5	54/109	+1.7%	6.7%	.79
Control	24		33.6	43/128	26.8	33/123	—6.8%	5.8%	.24
Net Change** (Consultation-Control)							+8.5%	8.9%	.32

*See ref. 46.
**See ref. 47.

TABLE 13
Unacceptable Values Reported

Determination and Group	Phase I			Phase III		
	Total No. Reports	No. > Acceptable Limits but ≤ ±20% of Target Value	Extreme Values No. > ±20% of Target Value	Total No. Reports	No. > Acceptable Limits but ≤ ±20% of Target Value	Extreme Values No. > ±20% of Target Value
True Glucose						
Criterion	136	26 (19.1%)	5 (3.7%)	140	19 (13.6%)	7 (5.0%)
Consultation	18	4 (22.2%)	0 (0.0%)	18	2 (11.1%)	1 (5.6%)
Control	28	4 (14.3%)	3 (10.7%)	29	4 (13.8%)	1 (3.4%)
Total Reducing Substance						
Criterion	51	3 (5.9%)	0 (0.0%)	51	5 (9.8%)	2 (3.9%)
Consultation	122	14 (11.5%)	8 (6.6%)	126	18 (14.3%)	4 (3.2%)
Control	119	19 (16.0%)	19 (16.0%)	116	6 (5.2%)	7 (6.0%)
Calcium						
Criterion	165	58 (35.2%)	5 (3.0%)	166	34 (20.5%)	3 (1.8%)
Consultation	68	29 (42.6%)	7 (10.3%)	70	27 (38.6%)	10 (14.3%)
Control	66	23 (34.8%)	14 (21.2%)	70	23 (32.9%)	7 (10.0%)
Chloride						
Criterion	189	14 (7.4%)	1 (0.5%)	190	18 (9.5%)	2 (1.0%)
Consultation	92	36 (39.1%)	6 (6.5%)	95	28 (29.5%)	0 (0.0%)
Control	100	25 (25.0%)	19 (19.0%)	105	25 (23.8%)	10 (9.5%)
Hemoglobin						
Criterion	196	23 (11.7%)	0 (0.0%)	198	18 (9.1%)	0 (0.0%)
Consultation	139	37 (26.6%)	1 (0.7%)	144	18 (12.5%)	0 (0.0%)
Control	155	32 (20.6%)	5 (3.2%)	149	35 (23.5%)	1 (0.7%)
Urea Nitrogen						
Criterion	183	30 (16.4%)	36 (19.7%)	185	32 (17.3%)	23 (12.4%)
Consultation	125	27 (21.6%)	67 (53.6%)	129	34 (26.4%)	36 (27.9%)
Control	148	29 (19.6%)	70 (47.3%)	142	25 (17.6%)	50 (35.2%)
Total Protein						
Criterion	182	104 (57.1%)	0 (0.0%)	185	92 (49.7%)	3 (1.6%)
Consultation	106	62 (58.5%)	21 (19.8%)	106	62 (58.5%)	11 (10.4%)
Control	114	66 (57.9%)	19 (16.7%)	114	63 (55.3%)	16 (14.0%)
Uric Acid						
Criterion	171	64 (37.4%)	12 (7.0%)	172	62 (36.0%)	10 (5.8%)
Consultation	69	18 (26.1%)	26 (37.7%)	73	26 (35.6%)	13 (17.8%)
Control	86	22 (25.6%)	28 (32.6%)	86	20 (23.3%)	15 (17.4%)
Cholesterol						
Criterion A	65	16 (24.6%)	3 (4.6%)	70	10 (14.3%)	4 (5.7%)
B	105	24 (22.9%)	53 (50.5%)	104	26 (25.0%)	36 (34.6%)
Consultation B	111	13 (11.7%)	81 (73.0%)	109	29 (26.6%)	45 (41.3%)
Control B	128	13 (10.2%)	91 (71.1%)	123	21 (17.1%)	72 (58.5%)

Continued

accuracy and precision ($P = <.001$ in each case via a Chi-square contingency table analysis with two degrees of freedom).[46] This indicates that supervision, as measured by the availability of a pathologist, is an important factor in determining the laboratory's ability to perform tests with a higher degree of accuracy and reliability.

Hospital Size: Chemistry Workload

Since laboratories throughout the state have various ways of recording work done, workload here was arrived at by summing the total number of hemoglobin determinations and the total number of chemical determinations on blood, plasma, or serum for the year 1962, and computing the average number per month. The workload figures were then grouped according to five categories and examined by means of regression analysis.[48] The results are given in Table 14, part 3a. The linear trends were significant for both accuracy and precision ($P = <.0005$ in each case).

Hospital Size: Bed Category

Laboratories had previously been classified according to hospital size as indexed by bed category for purposes of illustrating level of participation. Performance as it relates to bed category was also measured by regression analysis.[48] The results are given in Table 14, part 3b. The linear trends for both accuracy and precision were significant ($P = <.0005$ in each case).

Results for the two indices of hospital size indicate that the level of performance increases with the size of the hospital. This could be related to the greater likelihood of finding better-trained personnel in the laboratories of larger hospitals. Increased accuracy and precision also go hand-in-hand with carrying out laboratory tests at greater frequency. This is reflected in the larger workload categories.

Comments

Even though the relative importance of each factor could not be determined, it is interesting to note that laboratories showing top performance in each factor-comparison were, in general, the same laboratories. The smaller hospital laboratories, which were performing on the lowest level, also gave the poorest cooperation. These laboratories are staffed by personnel trained in commercial schools more often than larger laboratories, and as a rule are not supervised by pathologists.

Summary and Conclusions

An evaluation study in clinical chemistry involving 18 separate surveys was conducted by the Minnesota Department of Health in hospitals throughout the state. Ninety laboratories completed the study.

The purpose of the study was to determine:

1. Whether participation in an evaluative study over a period of time would cause improvement in laboratory results, and

2. Whether intensive consultation would be an effective means of upgrading laboratory results.

Laboratories were divided into three groups. The Criterion Group included the top-performing one third of the laboratories. The remaining two thirds were assigned to the Consultation or the Control Group. Accuracy and precision of eight determinations — glucose, calcium, chloride, hemoglobin, urea nitrogen, total protein, uric acid, and cholesterol — were measured for each group in each survey.

The Criterion and Control Groups were used to study participation. The results showed that participation in evaluation studies could bring about improved laboratory results for some determinations. The Control Group, however, did not approach the level of performance of the Criterion Group.

Intensive consultation was studied with the Consultation and Control Groups. Results indicated that consultation visits given to laboratories in the Consultation Group were effective in upgrading only one determination significantly, namely hemoglobin.

Laboratories were also rated according to three factors affecting laboratory results: level of training of personnel, availability of a pathologist, and hospital size (indexed by chemistry workload and bed category). Total

TABLE 14
Comparison of Over-All Performance with Personnel Training, Pathologist Availability, and Hospital Size**

Accuracy

1. TRAINING OF PERSONNEL

A. All Hospitals — Phase I

Category	Ratio*	Percent	P of Difference
ASCP	1385/2313	60.0%	<<.001
Other	435/937	46.4%	

B. Consultation and Control Groups — Phases I & III

Consultation

	Phase I		Phase III		P of
Category	Ratio	Percent	Ratio	Percent	Diff.
ASCP	210/446	47.1%	272/447	60.8%	<<.001
Other	183/404	45.5%	234/423	55.3%	.004

Control

	Phase I		Phase III		P of
Category	Ratio	Percent	Ratio	Percent	Diff.
ASCP	298/555	53.7%	359/568	63.2%	.003
Other	158/389	40.6%	162/366	44.3%	.30

2. AVAILABILITY OF A PATHOLOGIST

Category	Ratio	Percent	P of Differences
Yes	883/1378	64.1%	
Occasional	332/585	56.8%	<.001
No	605/1285	47.0%	

3. HOSPITAL SIZE

A. Chemistry Workload

Category	<250	251-500	501-1000	1001-5000	>5000
Ratio	442/984	379/689	306/537	455/686	238/354
Percent	44.9%	55.0%	57.0%	66.3%	67.2%
P of Differences			<.0005		

B. Bed Category

Category	<25	25-49	50-99	100-249	>249
Ratio	118/246	400/890	397/688	425/713	480/713
Percent	48.0%	44.9%	57.7%	59.6%	67.3%
P of Differences			<.0005		

Precision

1. TRAINING OF PERSONNEL

A. All Hospitals — Phase I

Category	Ratio*	Percent	P of Difference
ASCP	1514/2313	65.5%	<<.001
Other	452/937	48.3%	

B. Consultation and Control Groups — Phases I & III

Consultation

	Phase I		Phase III		P of
Category	Ratio	Percent	Ratio	Percent	Diff.
ASCP	237/446	53.1%	277/447	62.0%	.007
Other	216/404	53.5%	260/423	61.5%	.02

Control

	Phase I		Phase III		P of
Category	Ratio	Percent	Ratio	Percent	Diff.
ASCP	269/555	48.5%	336/568	59.2%	.001
Other	170/389	43.7%	154/366	42.1%	.65

2. AVAILABILITY OF A PATHOLOGIST

Category	Ratio	Percent	P of Differences
Yes	954/1378	69.2%	
Occasional	356/584	61.0%	<.001
No	656/1287	51.0%	

3. HOSPITAL SIZE

A. Chemistry Workload

Category	<250	251-500	501-1000	1001-5000	>5000
Ratio	497/984	404/688	326/537	473/686	266/354
Percent	50.5%	58.7%	60.7%	69.0%	75.1%
P of Differences			<.0005		

B. Bed Category

Category	<25	25-49	50-99	100-249	>249
Ratio	127/246	455/890	428/687	441/713	515/713
Percent	51.6%	51.1%	62.3%	61.8%	72.2%
P of Differences			<.0005		

*Ratio = total acceptable/total number of reports.
**See text p. 17 (following) for description of various categories.

Continued

performance scores for each laboratory were compared with each factor. The results showed that:

1. Laboratories employing well-trained technologists demonstrate a higher level of accuracy and precision than those employing less-well-trained laboratorians.

2. Well-trained technologists are capable of significantly improving laboratory performance by participating in evaluation studies, while less-well-trained laboratorians gain little or no benefit from participation.

3. Less-well-trained personnel are able to improve performance significantly when given intensive consultation.

4. Laboratories supervised by pathologists perform tests more accurately and precisely than those not supervised by pathologists.

5. The level of performance of a laboratory increases as bed category and workload increase.

In terms of the expense involved, the benefit gained from intensive consultation is questionable — at least on the short-term basis available in this study. The positive effect of consultation found for one determination does imply that this means of improving laboratory performance should be reexamined. In addition, the possible need for a continuing program to maintain the improvement in performance of the less-well-trained personnel should be studied. Future studies might well be devoted to discovering the most effective and economical methods for improving laboratory performance.

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12-48 May be obtained from the author or the reprints.

CASANOVA, the libertine, was told by a surgeon that he was indebted to him for his present comforts, and when he inquired why, the surgeon stated: "In this way, captain. You had a connection with Don Jerome's housekeeper, and you left her, when you went away, a certain souvenir which she communicated to a certain friend of hers, who, in perfect good faith, made a present of it to his wife. This lady did not wish, I suppose, to be selfish, and she gave the souvenir to a libertine, who in his turn was so generous with it that, in less than a month, I had about fifty clients."*

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*Massengill, S. E.: A Sketch of Medicine and Pharmacy, S. E. Massengill Co., Bristol, Tenn.-Va., ca. 1941, p. 42.

To "darn" your luck is not the best way to mend it. — Nuggets

Perinatal Mortality Study

Prolonged Labor—Uterine Inertia *

Case Report

This was the first pregnancy of this twenty-two-year-old mother. Prenatal care began during the second lunar month, and she had no illness during the pregnancy. At 36 weeks of gestation she entered the hospital emergency room because of periodic abdominal pains for two days and now occurring every fifteen minutes. A diagnosis of very early labor was made, and the patient was discharged, but she returned two hours later, at which time both the patient and her husband were very anxious.

Physical Findings

Examination on the return admission revealed the cervix to be 1-2 cm. dilated and 75% effaced. The periodic abdominal pains continued, but of poor quality, and 12 hours following admission the cervix was 4-5 cm. dilated. The fetal heart tones were normal. Pelvimetry on the day of admission showed a normal pelvis. Twenty-two hours following admission a vaginal examination revealed the cervix to be thin and 4-5 cm. dilated.

Therapy

The mother then received 100 mgm. intramuscular Librium which slowed the labor and relaxed her. Forty-four hours following admission the membranes ruptured and she was started on penicillin and streptomycin therapy.

Uterine Inertia

Three days after admission labor finally stopped altogether. A urinalysis done three days following admission showed 2 to 3 plus WBC, no albumin, no sugar, no casts or bacteria. No urine culture was done, but the physician started the mother on Gantrisan therapy for four days. Four days after admission the mother was moved to a nonmaternity floor, and the penicillin-streptomycin therapy was changed to Achromycin, 1 capsule four times daily. Five days following admission the mother had a yellow vaginal discharge. No smear or culture was done on the discharge. A vaginal examination done on the fifth day revealed the cervix to be 9 cm. dilated and station plus one.

Stimulating Labor

The mother was then given Tocosamine lcc. I.M., which caused no change. Nine hours after the Tocosamine, she had irregular contractions three to ten minutes apart. The cervix remained 9 cm. dilated and station plus one. The mother was then given intravenous pitocin drip (½ ampoule in 500 cc. glucose in water); after four hours of pitocin drip the contractions were four to 26 minutes apart and of poor quality. The position of the infant was occiput posterior, and the fetal heart tones were 130 to 160 per minute. It was now the sixth day after admission.

Low Forceps Delivery

The physician then used low forceps to deliver the occiput posterior infant under pudendal and paracervical block anesthesia. The fetal heart rate was 160 per minute one hour before delivery, 108 per minute one-half hour before delivery. After delivery the infant took only one or two gasps. Positive pressure oxygen and intubation were used on the infant to no avail, and it expired in less than one minute. No obstetric consultation was obtained at any time.

Autopsy Findings

Autopsy on the 6-lb. male infant showed the abdominal cavity to be filled with blood, estimated at approximately 60 cc. in amount. The capsule of the liver was torn in two places over the costal margin. There were subcapsular hematomas measuring up to 1 cm. in diameter adjacent to the liver capsule tears. Microscopic examination of the liver in the area of the capsule tears showed some early degenerative changes in the liver cells and some areas of hemorrhage into the parenchyma. Also, small hematomas were seen beneath the liver capsule.

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*Ramsey County Perinatal Mortality Study Committee.

The lungs did not float in water, and microscopic examination of them showed most of the alveoli to be collapsed. The remainder of the autopsy, including the brain revealed no areas of hemorrhage or abnormality.

The pathologic diagnosis was hemoperitoneum with laceration of the liver capsule and subcapsular hematomas.

Comment

The Ramsey County Perinatal Mortality Study Committee criticizes the care that the mother received as follows:

Unjustifiable Delay

A primary uterine inertia was not stimulated when no progress had been made in the twelve-hour and the twenty-second-hour examination. Stimulation, not relaxation (Librium) was indicated. Had *stimulation, amniotomy* and/ or Tocosamine or Pitocin failed, *the patient should have been sectioned* on the basis of "failed labor." The remainder of the management was indefensible, including the apparently traumatic delivery which was apparently the direct cause of perinatal mortality.

Plants Yield Tumor-Inhibiting Compounds

Podophyllotoxin has been obtained from *Juniperus virginiana* L. by S. Morris Kupchan, Jane Hemingway, and John Knox. An alcoholic extract of the leaves and twigs of the plant from Maryland was found to have inhibitory activity against Sarcoma 180 in mice and *in vitro* against human carcinoma of the nasopharynx carried in cell culture. (KB).

March '65, American Pharmaceutical Association, 2215 Constitution Avenue, N. W., Washington, D. C. 20037.

Post Hoc, Ergo Propter Hoc

The treatment of typhoid fever throughout the years has been variable and very interesting. An outstanding product used for a long period was antimony, which has no value in the treatment of the disease, but because it was given to Louis XIV and he seemed to improve following its administration, it became a favorite for years. Louis had been very ill with typhoid for a long time and showed no improvement with the usual concoctions of gold leaf suspended in wine, pearls dissolved in vinegar, and frequent poulticing. He was purged and bled, bled and purged and at last in desperation, his physician tried antimony. Louis was due to either die or get well and because the latter was in order, the antimony was given the credit.

— F. William Saul, M.D.: Pink Pills for Pale People

Life can only be understood backwards, but it must be lived forwards.

— Soren Kierkegaard

Medical Economics

Life Insurance Dividends

Since the average doctor carries approximately $70,000 worth of life insurance, the disposal of the dividends which his policies earn should be an important matter to him.

With regard to dividends, participating life insurance contracts usually provide the policy holder a choice among four options. (1) Under the "cash" option, dividends will be paid to him annually in cash. (2) The "premium' option provides that the dividends will be used annually as partial satisfaction of premium due. (3) The "paid-up insurance" option provides for the use of annual dividends for the purchase of paid-up additions to the life insurance policy. (4) The "interest" option provides for the deposit of dividends with the company to accumulate at interest.

In general, options No. 1 and No. 4 have little value for the doctor who is in the process of building up his life insurance program. Option No. 1 should be chosen only by the man whose policies are already paid up and who has no need for additional insurance. Option No. 4 lost its attractiveness when yields from other sorts of investments (even savings accounts in commercial banks) began to surpass the insurance companies' 2 or 2½ per cent, and besides, with most low-net-cost companies, the paid-up additions available under option No. 3 acquire a cash value which will equal or exceed the accumulation of dividends and interest over a period of years.

In general, option No. 4 would be worthy of consideration only on contracts permitting the conversion of accumulated dividends and interest to paid-up insurance at any time. Such a privilege is relatively rare today.

It is our feeling that options No. 2 and No. 3 are most worthy of consideration by the average policyholder. Option No. 2 should be elected by the young doctor who is building up a large insurance program and wants maximum protection. Obviously, he can buy much more insurance by paying only the net premium (premium less dividend), than by using dividends otherwise. Later, if his financial position improves or if he becomes uninsurable, he can change his election to option No. 3 (paid-up insurance) if he wishes.

Option No. 3 is generally best for a doctor between 40 and 50 years of age who does not have as much insurance as he should have or would like, and it is also quite valuable to the man who has become uninsurable. Men in these situations can elect to have their dividends purchase paid-up additions which will increase their protection and also maintain a cash value equal to, or slightly greater than, the sum dividends and interest would have provided them if they had been left on deposit. Thus, such men would have maximum protection, but still would retain a cash reserve for retirement or for emergency use.

What about doctors who elected years ago to leave their dividends on deposit? Such a man has a sizeable accumulation drawing 2 or 3 per cent taxable interest. His individual situation should be reviewed and probably his dividend option changed. If he needs protection through additional insurance, a paid-up insurance option should be taken on future dividends and — to the extent possible — on accumulated dividends.

To the extent that paid-up additions are prohibited on the accumulation, it is our feeling that these dividends can be withdrawn and profitably invested elsewhere. That course of action should also be chosen by the man whose insurance needs are declining. He can withdraw his dividends and reinvest them at a higher return.

Before making a decision on a matter of this sort, one should review his needs and his coverage with a competent insurance agent or analyst. He must consider his over-all financial position in relation to the options that are available under the particular contracts he owns.

If you have a dividend problem, you should consult a qualified advisor at once.

William D. Huntington*
Minneapolis, Minnesota

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*Northern Division Manager, Professional Management Midwest.

You cannot prevent the birds of sorrow from flying over your head, but you can prevent them from building nests in your hair. — Chinese proverb

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Meetings and Announcements

Whosoever is afraid of submitting any question, civil or religious, to the test of free discussion, is more in love with his own opinion than with truth. — T. Watson

JULY

Nineteenth Annual Rocky Mountain Cancer Conference, July 16-17, Brown Palace Hotel, Denver Colorado. Contact: Rocky Mountain Cancer Conference, 1809 East 18th Avenue, Denver, 80218. . .

Zumbro Valley Medical Society — Regular Meeting, July 1, 8:00 p.m., Plummer Hall, Mayo Clinic, Rochester.

Minnesota Surgical Society — Business & Program, July 16. Duluth, "Advances in Pediatric Surgery."

The 102nd Annual Meeting of the American Veterinary Medical Association will be held in Portland, Oregon, July 11-15. Portland's Memorial Coliseum. Contact: American Veterinary Medical Association, 600 South Michigan Avenue, Chicago 5, Illinois.

AUGUST

Southern Minnesota Academy of General Practice, Seminar, 3:45 p.m., August 24, LeSueur.

Minnesota Medical Foundation, Board of Trustees, 6:30 p.m., August 25, Place undetermined.

University of Wisconsin Medical Center three-day course on ongoing developments in surgery, August 26-28, at the Medical Center. Contact: Paul Knipping, 401 Extension Bldg., University of Wisconsin, Madison, Wisconsin.

American Academy of Physical Medicine and Rehabilitation, August 22-27, at the Sheraton Hotel, in Philadelphia. Contact: The Academy at 30 North Michigan Avenue, Chicago.

American Physicians Fellowship orthopedic seminar, August 4-15, in Israel. Contact: American Physicians Fellowship, 1622 Beacon Street, Brookline, Mass.

SEPTEMBER

Zumbro Valley Medical Society, September 1, Plummer Hall, Mayo Clinic, Rochester.

St. Louis Co. Medical Society, Executive Comm., September 9, 6:00 p.m., St. Mary's Hospital, Duluth and Regular Meeting, 8:00 p.m.

Minnesota Heart Association, Annual Meeting, Scientific Sessions, September 18, 9:00 a.m. — 5:00 p.m. (Place unknown).

Minnesota Medical Foundation, Annual Meeting, September 27, 8:00 p.m., Mayo Auditorium, University of Minnesota, Minneapolis.

ANNOUNCEMENTS

Hahnemann Medical College & Hospital, Philadelphia, postgraduate courses:

July 26-30 — Interpretation & Therapy of Cardiac Arrhythmias, Hahnemann CVI Bldg., Philadelphia.

Nov. 22-24 — Symposium Cancer Chemotherapy, Sheraton Hotel.

* * *

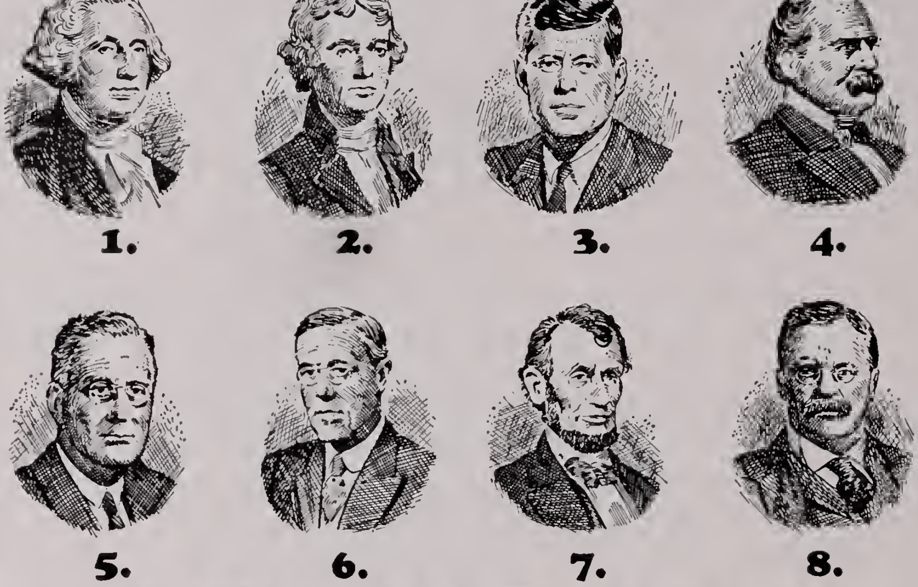
Three-day course directed to surgically oriented physician will be held at the University of Wisconsin's Medical Center, Aug. 26-28. Aspects of cardiovascular surgery, biliary tract surgery, and general abdominal surgery will be presented. Write: The University in Madison.

* * *

Next scheduled Part I (written) examination by the American Board of Obstetrics and Gynecology will be held at various examining centers on July 2, 1965 at 10:00 a.m. Applications received for next Part II examination to be given in Chicago in April 1966 will be reviewed in September and notification will be mailed October 1st.

* * *

The Renville-Redwood County Medical Society wishes to announce the winners in Renville County of the 1965 Association of American Physicians and Surgeons 19th Annual National Essay Contest for high school students. First place goes to Karen Halliday of Olivia; second place prize goes to Jim O'Malley, Olivia, and third place prize to Vickie Wiersma of Olivia.



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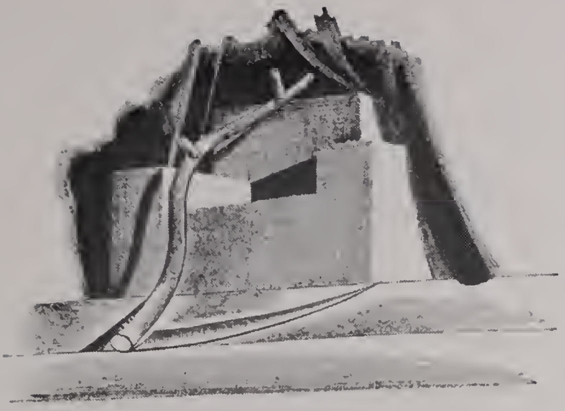

In Memoriam

This world is the land of the dying; the next is the land of the living.
— Tyron Edwards

ALVA E. HOLMES, M.D.

Dr. Alva E. Holmes, 86, Rush City physician, died February 26. He was born in Virginia City, Nevada, and received his degree in medicine from the Kentucky School of Medicine in Louisville, Kentucky.

He was a member of the American Medical Association and East Central Medical Society and a 50 Club member of the Minnesota State Medical Association.

He is survived by a sister in Culver City, California.

JOHN A. O'HANLON, M.D.

Dr. John A. O'Hanlon, 59, Minneapolis physician, died May 14th. A native of Minneapolis, Dr. O'Hanlon attended St. Thomas Academy and College prior to attending Marquette University Medical School, Milwaukee. He had been in private practice since 1949 and was chief medical officer of the Minneapolis Postoffice.

He was a member of the Hennepin County Medical Society, Minnesota State Medical Association, and American Medical Association.

He is survived by his wife, a daughter, and two sons.

HENRY C. OTTO, M.D.

Dr. Henry C. Otto, 79, resident of the Frazee-Vergas area for the past fifty-six years, died, April 27th. He was born on a farm in rural Nicollet county, but received his medical degree from the University of Louisville in Louisville, Kentucky.

Dr. Otto was a member of the Masonic Lodge No. 241 AF and AM, Scottish Rites bodies, Clay-Becker Medical Society, Academy of General Practitioners, American Medical Association, and life and 50 Club member of the Minnesota State Medical Association. He had been a member of the staff of St. Mary's hospital.

He is survived by his wife, a son and a daughter.

ROLF HOVDE, M.D.

Dr. Rolf Hovde, 72, physician and surgeon in Winthrop for forty-six years, died at his home, April 10th. He was born in Brookings, South Dakota, and moved with his family to Duluth when he was eight years old. He received his medical degree from the University of Minnesota and interned at the Hennepin County General Hospital in Minneapolis.

Dr. Hovde was a member of the American Medical Association, Southern Medical Association, Brown County Medical Society and Minnesota State Medical Association. He also served on staffs at Union and Loretto hospitals in New Ulm, Glencoe, Arlington and Gaylord. Activity in Masonic groups led to his attaining the highest office of the Knights Templar in Minnesota, that of Grand Commander.

He is survived by his wife, three sons and a daughter.

THOMAS E. FLINN, M.D.

Dr. Thomas E. Flinn, 80, Redwood Falls physician, died April 8, at the Redwood Falls hospital. He was born in Redwood Falls and graduated from the Rush Medical College, Chicago. He began the practice of medicine in Redwood Falls in 1911 and remained there until his retirement in 1946.

He was a member of the American Medical Association, Renville-Redwood Medical Society and a 50 Club and life member of the Minnesota State Medical Association.

He is survived by his wife, one daughter and two sons, one of whom is Dr. John H. Flinn of Rochester. Another son, Dr. William C. Flinn, was killed in an accident in France in 1945.

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History of Medicine
IN WRIGHT COUNTY

JOHN J. CATLIN, M.D.
Buffalo, Minnesota

ROBERT ROSENTHAL, M.D.
St. Paul, Minnesota

Editors Note: Article continued from June 1965 issue of Minnesota Medicine.

Rufus L. Thurston, a homeopath, was at South Haven for a short time. He was licensed in Minnesota as a homeopath August 23, 1884. He was a graduate of the Hahnemann Medical College of Chicago in 1882. In 1890 he is listed in Minneapolis, from 1895 through 1909 in Boston, Mass.

Gilbert H. Tollington, practiced in Clearwater from about 1890 through 1898. He was one of four physicians there in 1890 when Clearwater had a population of about 400; while in 1893 and 1896 only he and Dr. I. L. Edmunds are listed there, when the population was below 300. All in all it seems that he was in Clearwater about ten years as he left that town before the turn of the century. Dr. Ira Leslie Edmunds was one of the physicians in Clearwater at that period and a St. Cloud newspaper item of July, 1896 mentions that Drs. Tollington, Edmunds and Ridgway did surgery together at the St. Raphael's Hospital in St. Cloud. During the first decade after the turn of the century he practiced in Minneapolis.

He was a graduate of the College of Physicians and Surgeons, Chicago in 1885 and was licensed in Minnesota April 28, 1887. He was the son of Thomas and Sarah Tollington. His sister, Ann Jane, married Dr. I. L. Edmunds.

A "**Dr. Trow** of Cokato" opened his large residence for use as an emergency hotel after the regular hotel burned down. Nothing more could be learned about him; it could not even be ascertained that he actually was a physician.

Sidney R. Wakefield, a homeopath, came to Minnesota in 1866 and settled in Monticello. He was born in Trumbull County, Ohio April 18, 1822 and graduated from Willoughby Medical College, Willoughby, Ohio in 1846. During the Civil War he served as assistant surgeon in the 71st Ohio Volunteer Infantry Regiment and came to Minnesota after the war. He was a founder and a signer of the Articles of the Minnesota State Homeopathic Institute when it met in 1867 at the Globe Hotel in St. Paul.

In 1871 Dr. Wakefield advertised "special attention paid to surgery of all kinds, also to chronic diseases, pulmonary and throat affections, and all their diseases and maladies."* At that time his office was located over T. G. Mealey's Dry goods and grocery store. It seems he moved away again as we learn early in 1881 that Dr. Wakefield's "goods and chattles have arrived. The doctor's family is expected daily." In May his family had joined him.

He was now one of three doctors in Monticello, the others being Drs. Gibbs and Smith. By June he had rented a house and was ready to start

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*The Northern Statesman (Wright County) February 4th, 1871.

Continued

practice.* He may have done coroner's services as in November 1884 his claim of $13.40 for an inquest was approved by the county.

He was licensed in Minnesota December 31, 1883. He was listed as practicing in Monticello through 1900 and apparently had an extensive rural practice. He was a charter member of the Wright County Medical Society when it reorganized in 1894 under this new name. The organizational meeting was held August 1 in the parlor of the American House at Buffalo, Dr. Wakefield calling the meeting to order. He was elected vice president. Dr. Wakefield died December 13, 1916 in the home of his son in Creswell, Oregon, of "senile debility" at the age of almost ninety-five.**

He probably was a relative of Dr. Kee Wakefield of Hutchinson, McLeod County, who practiced there in the 1880's and visited Monticello in 1881.

Clement A. Westholter, practiced in St. Michael from 1896 through 1900. While there he built a large house in the country toward Albertville. He tried to establish a "Water Cure" and it seems he was more interested in establishing and running a cure for chronic diseases than to have a regular practice. St. Michael apparently attracted him because of its German community, but he was not able to succeed there as a physician.

Dr. Westholter was born in Hamm, Westphalia, Germany and received his medical education at the University of Paderborn (1878). He practiced in Gottingen for three years before coming to the United States in 1882. Here he practiced in Tatopolis, Illinois and Indianapolis, Indiana. He was licensed in Minnesota April 14, 1896 and practiced in this state in St. Michael, in Buckman, Morrison County, and Albany, Stearns County. He died in Albany in 1921. He was married and had twelve children.

Jarid D. Wheelock, was a very early pioneer physician of Wright County. He came to Clearwater in 1855 as the first physician to settle in Wright County. He was licensed in Minnesota by exemption (under the "years of practice" section of the act) November 28, 1883.

In the early 1870's he was associated with Dr. Collins and the card of "Wheelock and Collins," appeared for half a year in the *Wright County Times* of 1875. In Clearwater he is listed as late as 1890 (but no longer in 1893). In 1890 Clearwater had a population of about 400 and there were four physicians (Drs. Edmunds, Munger, and Tollington besides Dr. Wheelock).

Dr. Wheelock was born in Montpellier, Vermont September 28, 1820.† He studied medicine at the College of Woodstock, Vermont. He died September 11, 1891 at the age of seventy-three.‡ A St. Cloud newspaper carrying the death notice, states that twenty-five or thirty years ago he was a resident of St. Cloud (this must have been in the 1860's)§ and he moved from there to Clearwater. It also recalls that he was a highly esteemed and skillful physician. Dr. Wheelock was also interested in farming.

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*Wright County Eagle, February — June 1881.

**James Eckman, "Homeopathic and Eclectic Medicine in Minnesota," Minnesota Medicine, November, 1941, p. 971.

†Upham and Dunlap "Minnesota Biographies, 1655-1912."

‡If his birthdate is correct he was only 71 at the time of his death.

§It seems he was in St. Cloud in 1865, and then was in partnership with Dr. M. C. Talman.

(To be Continued Next Month)

Conscience is the still small voice that makes you feel even smaller.

— Herbert Prochnow

Physician's Diary

In poverty and other misfortunes of life, true friends are a sure refuge — The young they keep out of mischief; to the old they are a comfort and aid in their weakness, and those in the prime of life they incite to noble deeds. — Aristotle

Dr. Fred D. Roth was elected president of the Mankato Clinic, Ltd. recently. Other officers are: **Dr. John J. Heimark**, vice president; **Dr. Chester E. Thiem**, secretary, and **Dr. A. A. Schmitz**, treasurer.

* * *

Dr. J. C. Swan, Mayo Clinic heart specialist and director of St. Mary's hospital cardiology laboratory, is to become chief of cardiology at the new Cedars Sinai Medical center in Los Angeles.

* * *

Dr. J. E. Nord and **Dr. Phillip Parker** of Staples were honored at an appreciation dinner recently by the people of Staples. **Dr. Nord** is leaving Staples and will relocate in Ada.

* * *

Dr. O. H. Beahrs, head of a section of surgery in the Mayo Clinic, was elected president of the Society of Head and Neck Surgeons at the annual meeting of that organization at San Juan, Puerto Rico.

* * *

Dr. James N. Kvale has opened up a practice in Atwater.

* * *

Dr. G. E. Lee has been reappointed chief of the medical staff of Glenwood Community hospital at its annual meeting. **Dr. B. A. Kolp** was appointed vice president and **Dr. R. R. Frear** of Brooten, secretary-treasurer.

* * *

Dr. Gordon Seagrave, the famed "Burma surgeon" died at his Namkham hospital last March. MINNESOTA MEDICINE published an article on **Dr. Seagrave** and his tremendous work in Volume 46:595, 1963.

* * *

Drs. A. L. Vadheim and **F. N. Thomsen** were recently made honorary members of the medical staff of the A. L. Vadheim Memorial Hospital in Lake Benton.

* * *

Dr. John C. Duffy, a Fellow at the Mayo Clinic, Rochester, Minnesota won the 1965 Grand Award of $500 in the "In My Opinion" competition cosponsored by the Student American Medical Association and Wyeth Laboratories at Radnor, Pennsylvania.

* * *

Dr. Robert V. Hodapp of Willmar has been appointed to the advisory committee on health and physical education of the Minnesota State Department of Education.

* * *

Dr. Jan Tillisch, Mayo Clinic section head, who has been ill in Athens, Greece, has returned to Rochester and is recovering satisfactorily.

* * *

Dr. Douglas J. Coy, Grand Rapids Clinic, and **Dr. Robert P. Balderson**, Itasca Memorial hospital, addressed the Range Medical Society at its April meeting. Their subject was "Non-malignant Diffuse Thyroid Disease."

* * *

Minnesota has more volunteer-physicians who have spent time on the HOPE ship than any other state except a few of the larger ones like New York. Fifteen have gone from Minnesota, twelve from the Twin Cities. Also, a bigger response to an appeal for funds comes in each year from Minnesota.

* * *

Dr. Walter H. Fink was honored at a dinner given for him by fellow members of the Minneapolis Ophthalmological Society at the Minneapolis Club on April 20th. **Dr. Fink**, who recently retired after forty years practice of ophthalmology in Minneapolis, was the founder of the Society.

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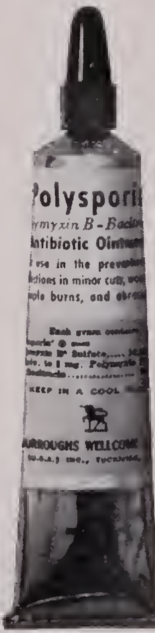

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References: 1. Carpenter, E. B., South. M.J. 51:627, 1958. 2. Crookshank, J. W.: J. Louisiana State Med. Soc. 114:272, 1962. 3. Feinberg, I., et al.: Am. J. Orthoped. 4:280, 1962. 4. Fitzgerald, W. J.: Miss. Valley M.J. 82:146, 1960. 5. Forsyth, H. F.: J.A.M.A. 167:163, 1958. 6. Meyers, G. B., and Urbach, J. R.: Penna. M.J. 64:876, 1961. 7. Truitt, E. B., Jr., Morgan, A. M., and Nachman, H. M.: South. M.J. 54:318, 1961. 8. Weiss, M., and Weiss, S.: J. Am. Osteopath. Assn. 62:142, 1962.

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BUSY, GROWING aggressive 3-man partnership in Northwest Wisconsin serving a trade area of 15,000 needs a well-trained recent graduate with fulfilled military obligations to associate immediately on excellent salary, with partnership in 1 year if mutually agreeable. Modern 15 room air conditioned brick clinic building is being doubled in size this year. 32 bed hospital and new 42 bed nursing home one minute from clinic. New 1500 student consolidated school. Excellent hunting, fishing and outdoor sport facilities in immediate area. Contact: MINNESOTA MEDICINE — 317; 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED LOCUM TENENS: multi specialty group desires pediatrician for one year. Salary open. Contact — Northwestern Clinic, Crookston, Minnesota.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE — 289; 496 Lowry Medical Arts Building; St. Paul, 55102.

WANTED: Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty seven bed hospital, X ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact: A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

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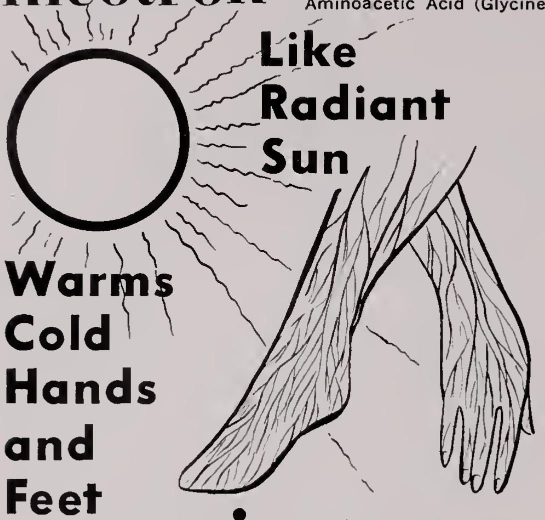
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1. Goodgold, J., Use of Nicotinic Acid-Glycine Mixture in Treatment of Peripheral Vascular Disease, Clinical Medicine 7:12 (1960).
2. Gustafson, Jr. et al. Use of Glycine in the Treatment of Peripheral Vascular Disease, Surgery 25:539 (1949).

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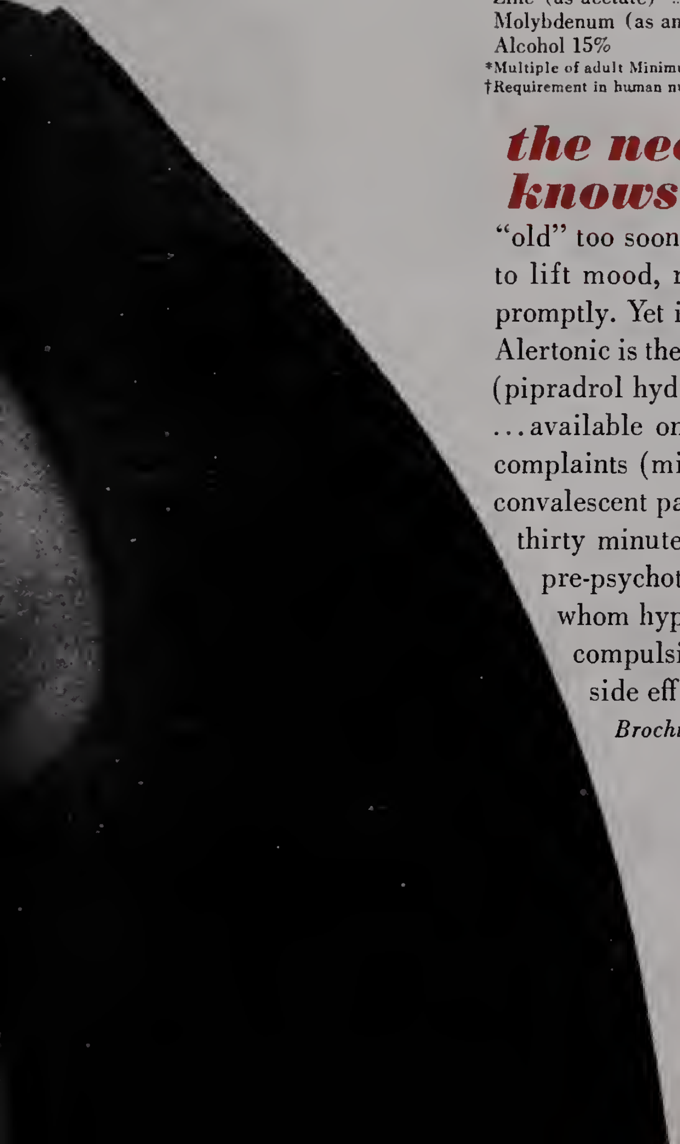

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*Dorhout Mees, E.J., and Geyskes, G.G.: Acta med. scandinav. 175:703,1964.

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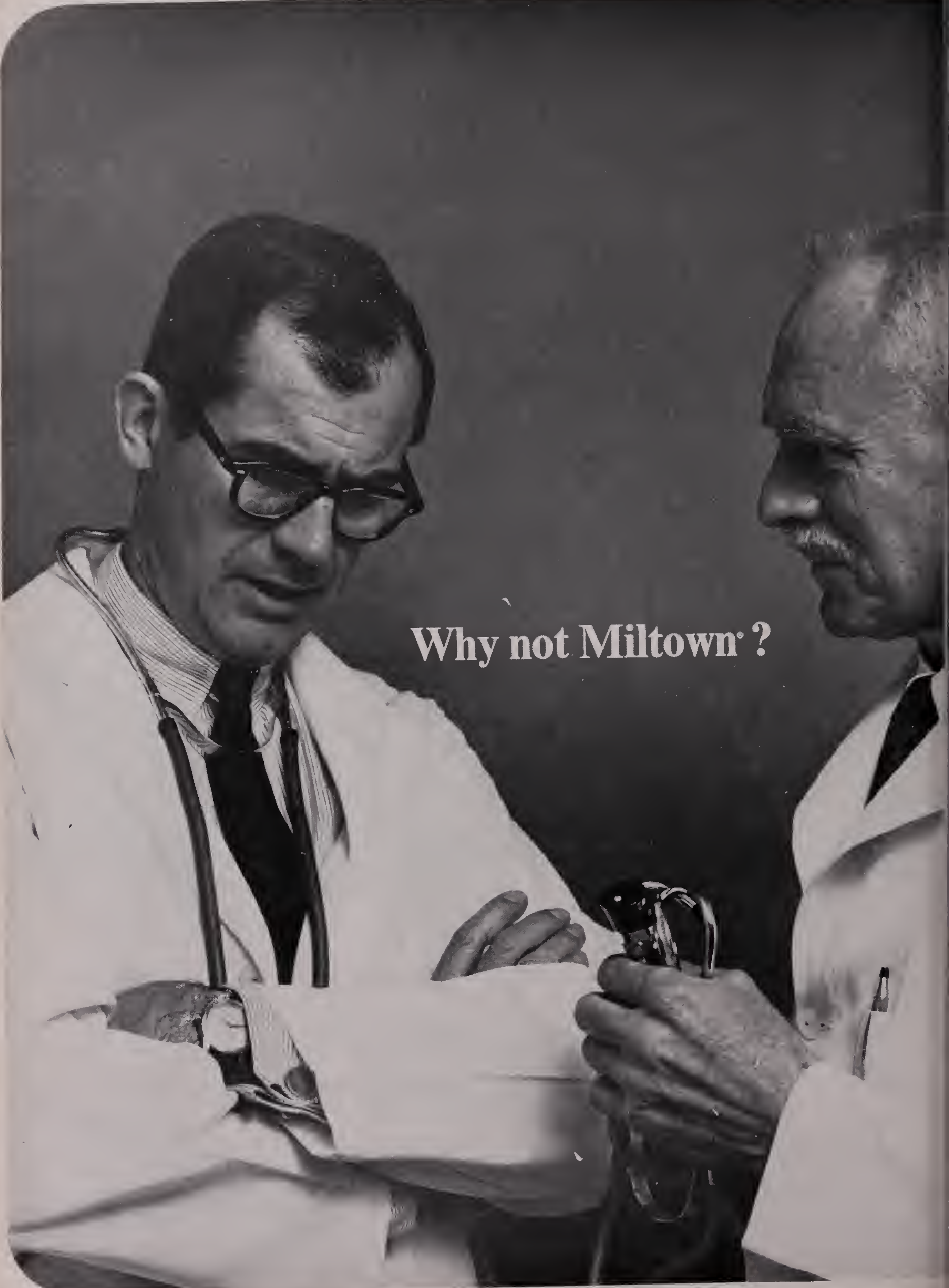
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Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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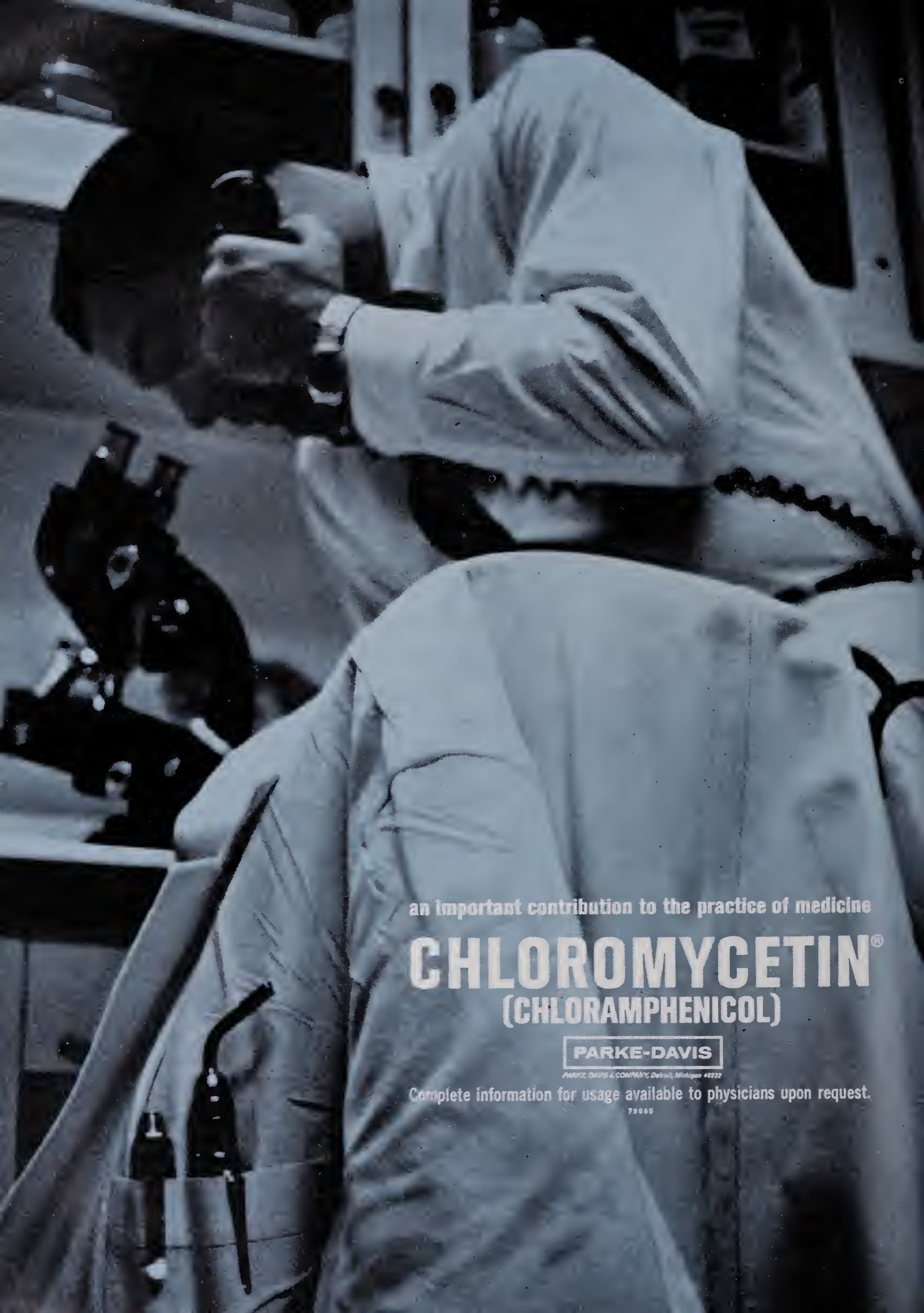

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President's Letter

This letter is being written at the close of another successful state medical meeting, and there are many to whom we owe our thanks. First, I would mention the Committee on Scientific Assembly which began its meetings last August and arranged an outstanding program. It was stimulating to see so many physicians at all the sessions and especially to note the interest in the panels emphasizing the psychologic and religious implications of medical practice. To all of the speakers, discussion leaders, and exhibitors we are grateful. Likewise, the many committees on local arrangements are to be congratulated, and we can never overlook the good work of the state office staff. For the benefit of the members of the various committees which met for breakfast discussions, I am recommending that special attention be paid in the future to obtaining facilities which will be more private and quiet for their deliberations which are such an important part of our work. A two-day meeting necessitates some condensation of the committee program.

In the House of Delegates there were two actions which I consider of great significance. One was the overwhelming vote to discard any expression of non-participation in proposed government plans for the care of patients over 65. This establishes our policy for the present and in no way obviates continued opposition to government control, while adhering at the same time, to principles involved in caring for all, regardless of need. The other significant event was the agreement by Minnesota Blue Shield to implement the major proposals of the Ad Hoc Committee to study that organization, which were approved by the House. With a closer working relationship assured, we look forward to a new era of successful operation of Blue Shield. An important feature is the agreement to promote the usual and customary fee as a basis for payment to the physician. If our experience with Medicare for servicemens' dependents is accurate, we can predict that Minnesota physicians will be cooperative in fulfilling the spirit of this concept. The success of the "usual fee" plan will require continued study so that we may thoroughly establish this important principle in all contracts with third parties, including the State Welfare Department. Percentage discounts for those patients in some income categories will be necessary, but with one fee schedule, the economic principles upon which the physician works will be much clearer.

Congratulations go to Dr. Peers Buckley, the president-elect, who comes to office with an unusually broad background of state medical activity. He will welcome, I am sure, any suggestions concerning the content and the length of the 1966 meeting in Duluth. Again, thanks to all who made the 1965 meeting an outstanding event. We anticipate similar support next year.

J M Stickney M.D.

J. M. Stickney, M.D.
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Collapsing Hip Nail

A Review of 132 Patients

Treatment of hip fractures has improved with use of a collapsing hip nail. One hundred thirty-two patients are reviewed in this article and results indicate superior function and rehabilitation with this device.

RUSSELL H. HARRIS, M.D.*
GILBERT F. MUELLER, M.D.*
JOSEPH C. KISER, M.D.*
THEODORE A. PETERSON, M.D.*
MALVIN J. NYDAHL, M.D.*
CLAUDE R. HITCHCOCK, M.D., Ph.D.*
Minneapolis, Minnesota

THE SLIDING NAIL is a valuable and workable adjunct in the treatment of hip fractures, especially those of the femoral neck. The experience at the Minneapolis General Hospital using the Massie Sliding Nail indicates that the rate of aseptic necrosis and/or nonunion following femoral neck fractures is less than can be expected using other methods of fixation.

The most common fractures requiring operative treatment are those involving the hip. Historically, prior to Whitman's classic presentation in 1920 of nearly 90 per cent healing in femoral neck fractures treated by adequate reduction and prolonged casting, this injury bore the stigma of a major tragedy, most certainly portending a prolonged disability and often death to the unfortunate elderly patient.[1] In 1931 Smith-Peterson introduced the well known triflanged nail as a method of internal fixation. This method of treatment significantly altered the concepts of therapy and remains today as a common method of fixation. Results using the Smith-Peterson nail vary from 60-85 per cent satisfactory union.

The Telescoping Nail

Dr. William K. Massie of Lexington, Kentucky, has recently devised a telescoping nail designed to avoid some of the common complications involved in operative methods of treatment for fractures of the hip.

Advantages

The theoretical advantages of this nail are: (1) Angle of the nail — 150°; (2) Telescoping device permitting impaction of the fracture; (3) Maximum purchase in the femoral head; (4) Early ambulation; (5) Single nail size.[2,3]

---

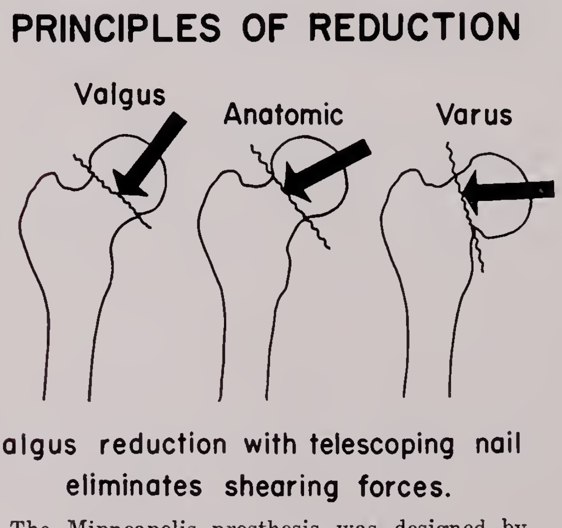
*Department of Surgery, Hennepin County General Hospital, Minneapolis (Formerly Minneapolis General Hospital).

Accurate reduction is of great importance for the proper utilization of the Massie nail. The head must be in anatomic or slight valgus position with the medial trabeculae of the femoral neck and head at an angle between 160 and 180° with the medial femoral cortex in the anteroposterior plane. The trabeculae should be at 180° in the lateral projection. This fracture is then subjected essentially to a compression force,[4] thus eliminating to some degree the shearing forces which tend to retard healing.

Following insertion of the nail and release of traction the nail collapses to some degree in the majority of cases, a feature which eliminates penetration into the acetabulum as impaction at the fracture site continues.

Results

Dr. Massie reported 90-per cent healing using this nail in the treatment of femoral neck fractures. The greatest test of any new form of treatment is its efficiency in the hands of others. We, therefore, have analyzed our series of Massie nail fixations done at Minneapolis General Hospital by residents and occasionally by interns under resident supervision. We began using the Massie nail in 1959 and since then have used it in over 160 patients. Our presentation here centers on 132 patients, with follow-up of one to three and one-half years. Of these, 84 were intertrochanteric fractures and 48 femoral neck fractures, in patients ranging in age from 44 to 101, with a median age of 70.


PRINCIPLES OF REDUCTION
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Valgus reduction with telescoping nail eliminates shearing forces.

Femoral Neck Fractures

Forty-eight of the 132 patients had femoral neck fractures, all of which were displaced high neck or intracapsular fractures. None of these cases could be considered undisplaced or abducted impacted fractures. All cases required reduction. In this group of 48 patients there was one postoperative mortality. Two additional patients died of unrelated causes before healing had taken place. Three developed avascular necrosis with bony union one to two years following injury. One patient had a failure of fixation, in which the nail retracted from the head twice and required insertion of a Minneapolis prosthesis.* One had a nonunion at 10 months which was felt to be caused by a poorly placed nail, and another was lost to follow-up. Excluding the patient lost to follow-up and the two patients who died of unrelated causes, thirty-nine (87 per cent) are considered to have excellent results at this time.

We recognize that the avascular necrosis rate in this series is incomplete, since only 75 per cent of our patients have been followed two or more years and none for longer than three and one-half years. A more critical analysis of this problem must await a longer follow-up period; but results to date have been very encouraging.

Intertrochanteric Fractures

Eighty-four of the 132 patients suffered intertrochanteric fractures, all of which were displaced and required reduction. Four were fractures of the extreme base of the neck. There were no subtrochanteric or pertrochanteric fractures included in this group. Nine of these 84 patients had severely comminuted fractures. There were four postoperative deaths. Three patients died of unrelated causes prior to complete healing. In one patient the nail broke immediately below the flange sometime between four and six months post fixation.

The Minneapolis prosthesis was designed by a group of orthopedic surgeons of the Twin City Orthopedic Society. It is formed of one piece of metal and has an 8-in. tapered, flanged stem designed to engage the anterior curve of the femoral shaft for stabilization.

Pain increased, and by one year post fracture a nonunion was present, and a Minneapolis prosthesis was implanted. One patient with an extremely comminuted fracture fully collapsed the nail by the second postoperative day, and it penetrated through the acetabulum one inch. This fracture healed and the patient enjoys painless weight bearing. One patient developed wound infection which healed uneventfully. Excluding three patients who died from unrelated causes, 73 (91 per cent) are considered to have excellent results.

TABLE 1
Femoral Neck Fractures

48 Patients	
Lost to Follow-up	1
Died of Unrelated Causes	2
45 Patients with Follow-up	
Avascular Necrosis	3
Failure of Fixation	1
Nonunion	1
Operative Mortality	1
Failures	6
87% Good Results	

TABLE 2
Intertrochanteric Fractures

84 Patients	
Lost to Follow-up	0
Died of Unrelated Causes	4
80 Patients Followed	
Operative Mortality	4
Broken Nail	1
Nail Penetrated	1
Failures	6
93% Good Results	

Comment

Our general over-all management of these patients has evolved slowly over a period of years in conjunction with the management of fixation with other types of nails. In general our contraindications to immediate surgery are conditions which can be expected to be remedied with 24-48 hours of medical management. These include: (1) Severe sepsis; (2) Cardiac dysrhythmia; (3) Extreme dehydration. With these few exceptions we feel that operation is indicated at the earliest possible time. Many of these patients undergo manipulation and fixation as an emergency procedure at night or on weekends.

Our postoperative management is directed toward prevention of medical complications inherent in this age group. This includes: (1) Early ambulation, (ordinarily the patient is sitting on the edge of the bed or in the wheelchair 24 hours after surgery). Instruction in gait training and parallel bar-walking progressing to crutch-walking is instituted 48 hours after surgery in patients where crutch-walking is felt feasible; (2) Nonweight bearing is advised for at least six weeks in the uncomplicated intertrochanteric fractures, or until there is X-ray evidence of healing in the femoral neck fractures. We find, however, that many of our patients start weight bearing immediately, and many walk without crutches after four weeks. Our patients are followed at monthly intervals until the fracture is healed clinically and by X ray.

Measurements made during healing have pointed out the advantage of the telescoping principle. The greatest measure of collapse in these fractures has been 2½ cm. In eight of our patients with fractured femoral neck and in 15 with intertrochanteric fracture, impaction at the fracture site was sufficient, so that, had rigid fixation been used, the nail would have penetrated the acetabulum.

Summary

We have reviewed 132 patients with fractured hip treated with the Massie collapsing nail. Of 48 with femoral neck fracture 87 per cent obtained good results; of 84 with intertrochanteric fracture 93 per cent obtained good results.

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Gastric

Volvulus of the stomach appears to be a rare condition. It may, however, occur more frequently than is generally supposed and every physician should be aware of this condition and should consider it in a differential diagnosis of acute upper abdominal disease.

The condition has been known since Berti,[1] in 1866, reported a case discovered at autopsy, in which a stomach had twisted two complete turns. In 1895 Berg[2] reported surgical treatment of a case. Since then a considerable number of cases have been reported, and in 1954 Gottlieb, Lefferts and Beranbaum[3] found 192 cases in the literature and added 20 of their own.

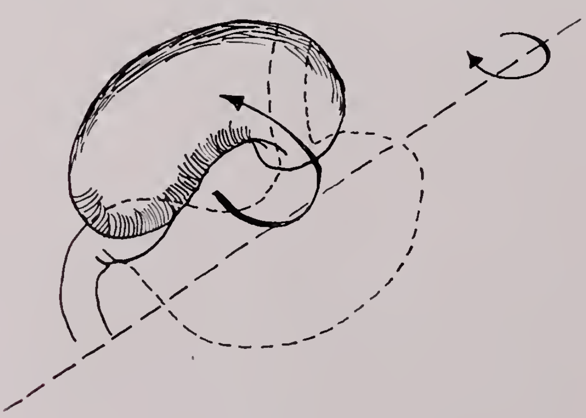

Figure 1

In 1956 Sawyer, Hammer and Fenton[4] added seven cases and pointed out that many of the previously reported cases were not true volvulus and should have been called potential, or incomplete volvulus, since the twist did not produce complete obstruction. In 1963 Guernsey and Connolly[5] added two cases in their excellent collective review and stated that about 200 cases of gastric volvulus had been reported in the literature, although many of these are probably not complete.

The condition appears to occur with equal frequency in males and females and may appear at any age, although it is most commonly seen in the age period between 40 and 60. It should be especially looked for in patients who develop severe upper abdominal symptoms after having had a traumatic rupture of the diaphragm.

The etiology of the condition is related to the anatomy of the region. It appears obvious that volvulus cannot occur unless the mesenteric attachments of the stomach are relaxed and elongated, especially in the region of the pylorus. This is usually congenital

---

*Department of Surgery, Quain and Ramstad Clinic, Bismarck, N. D.

Volvulus

R. F. NUESSLE, M.D.*
Bismarck, North Dakota

in origin and is often associated with ptosis of the stomach. Other factors which have been considered to contribute to the etiology include over-distention of the stomach, herniation or eventration of the diaphragm, gastric or extra-gastric tumors, ulceration of the stomach or duodenum. Traction by an over-distended colon or by a mobile spleen have also been considered to be possible factors in some cases.

Two main types have been described: the organo-axial and the mesenterial-axial. It is probable that not infrequently a volvulus of the stomach may represent both types.

In organo-axial volvulus a twist or rotation occurs about the longitudinal axis of the organ, that is, around a line roughly extending from pylorus to cardia. The greater curvature rotates, usually anteriorly, until it comes to lie above and in front of the lesser curvature and against, or above, the liver. The colon may come to lie stretched tightly across the posterior surface of the stomach (now facing anterior) and interposed between the diaphragm and the liver. When the twist exceeds 180 degrees, both pylorus and cardia may be expected to be obstructed (Fig. 1).

In mesenterial-axial volvulus, the twist occurs about a more or less vertical axis at right angles to the cardiac-pyloric line. The volvulus may be clockwise or counter-clockwise.

The initial effect of the volvulus is to close the pylorus by a kink or twist. The stomach is then unable to empty and begins to distend (Fig. 2). As the degree of rotation increases, the pylorus moves toward the fixed cardiac end of the stomach, folding the mid-portion of the stomach and causing a constriction (Fig. 3). As the twist and distention increase, the fold becomes a constrict-

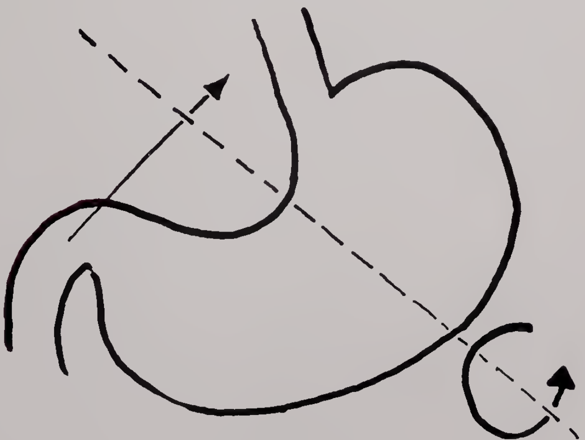

Figure 2

ing ring dividing the distended stomach into two sections. When the torsion has increased to the point where the two orifices are approximated, they form a pivot about which the further twisting of the organ occurs, obstructing the cardia (Fig. 4). At and beyond this point, the vascular supply of the stomach is endangered and may become occluded, producing strangulation. Patients in whom this occurs are extremely ill and are in peril of their lives unless the condition is quickly diagnosed and promptly treated surgically.

The symptoms are those of a high intestinal obstruction. The onset is often dramatic and sudden with severe expanding epigastric pain, often radiating through to the back, associated with a rapid onset of shock, distention and upper abdominal tenderness. At first the vomiting may be profuse, but it is shortly followed by retching and attempts to vomit without result. Ingesta are quickly rejected and attempts to pass a stomach tube are unsuccessful. These symptoms may be described as a triad: (1) attempts to vomit without result; (2) circumscribed upper abdominal pain, associated with upper abdominal and left hypochondrial* distention; (3) inability to pass a gastric tube.

In a true or complete volvulus of the stomach, x-ray examination will show distended loops of bowel in the upper abdomen and left hypochondrium, characteristically with two fluid levels. There is a malposition of the greater curvature and absence of the splenic shadow. If a barium swallow is given, the barium may not enter the stomach, and a characteristic, pointed shadow is often seen in the area of the cardia. If the cardia is demonstrable there will be found to be a low esophagogastric junction. In one of our cases the barium entered the upper portion of the fundus but could not fill the body of the stomach because of a constriction in the mid-portion of the stomach formed by the twist.

The treatment is surgical. At operation the volvulus is reduced. In some instances it may be necessary to perform a gastrotomy to relieve the gastric distention before derotation of the volvulus is possible. When derotation has been accomplished, a nasogastric tube can be manipulated into the stomach which can then be emptied. Various procedures for prevention of recurrence of volvulus have been attempted, including

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*See Test Your Word Score Page 1029.

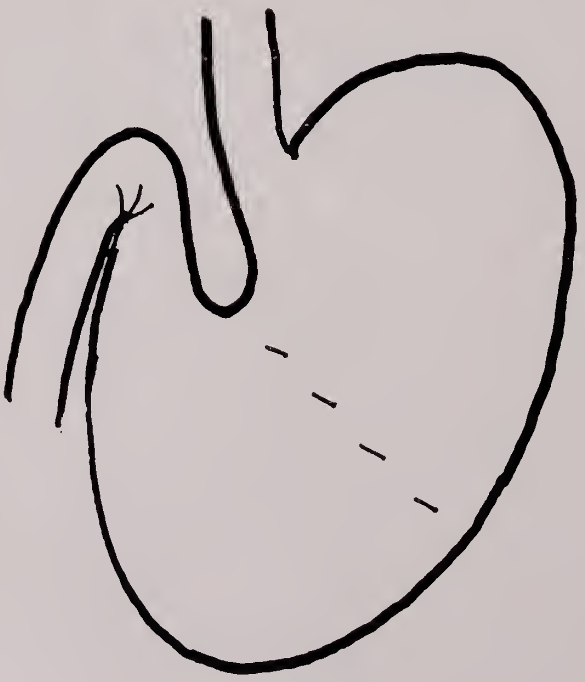

Figure 3

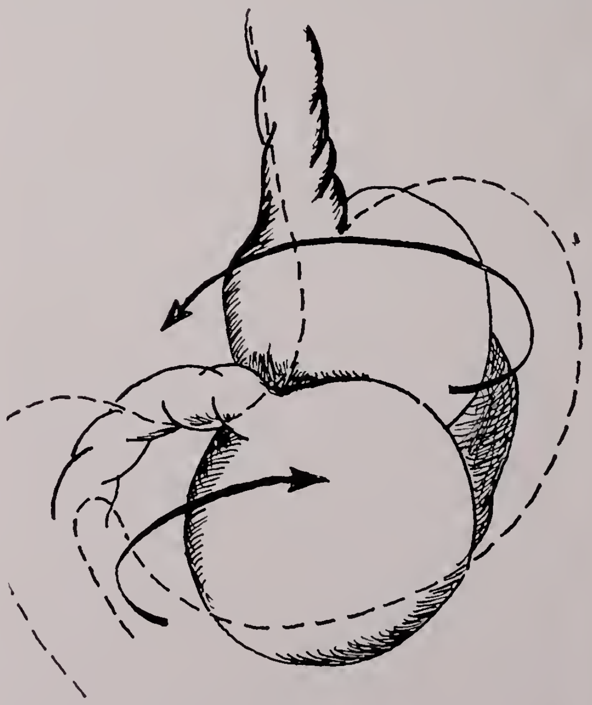

Figure 4

gastropexy, gastrectomy and gastroenterostomy. It is essential that the stomach be kept decompressed for several days after surgery and that investigations be made to rule out the possibility of duodenal ulcer or gastric carcinoma before the patient is discharged.

Case Histories

The following two cases illustrate two forms of the disease.

Case # 1

An 80-year-old white female was referred by her local doctor because of severe abdominal pain and distention for one day. The patient stated that she had been entirely well until 7 o'clock the evening before when she stooped over and suddenly noted severe abdominal pain. The pain had increased progressively, together with increasing distention of the abdomen. There had been nausea without vomiting and she had been obstipated. Previous similar symptoms were denied.

Examination revealed a rather feeble, moderately obese woman who appeared to be acutely ill. General examination did not reveal any abnormal findings except in the abdomen, which was markedly distended, mostly in the left lower quadrant. There were no masses or tenderness, and peristalsis was absent. Rectal and pelvic examination revealed no abnormality. The leukocyte count and hemoglobin were normal.

Roentgenograms of the abdomen showed a markedly distended viscus occupying the left abdomen and containing a fluid-air level. Above, and to the left of this viscus, was another gas and fluid-filled cavity with a fluid level. On the decubitus views the two cavities were separated by a short band of soft tissue. Gas-filled large bowel loops were evident on the right between the liver and the diaphragm, but only a small amount of gas was seen in the sigmoid colon. A diagnosis of volvúlus of the stomach was made by the roentgenologist.

At operation through an upper left paramedian incision, the large and small bowel were seen to be collapsed, but the stomach was cyanotic and edematous and showed tremendous distention, almost filling the abdomen. There was some serosanguineous fluid in the upper abdomen. The spleen lay anterior to the stomach, beneath the xiphoid and anterior to the liver at the mid-line, the stomach having been rotated in a counter clockwise direction. The pylorus and antrum had rotated to the left behind the cardia and were found high beneath the left diaphragm, from which they were reduced with some difficulty. Then, however, it was possible to derotate the stomach quickly and return the spleen and greater curvature to their normal location. The cardia, esophagus and duodenum appeared normal although redundant. The greatly distended stomach contained both fluid and air. The previously placed Levine tube had been advanced only to the lower esophagus, and, with the anesthetist working above and the surgeon below, it was finally possible to pass the tube into the stomach, after which 1,600 cc. of fluid and a like amount of air were evacuated from the stomach. The stomach and bowel being replaced in the normal position, the abdomen was closed in the usual manner without any other procedures.

The patient was maintained on nasogastric suction for four days, after which her recovery was uneventful.

A year later she stated she was entirely well and denied any gastrointestinal symptoms. Her general examination was normal. A roentgenogram of the stomach at this time showed chronic duodenal deformity, presumably due to scarring, since no ulcer crater could be demonstrated.

Case # 2

A 70-year-old female was seen because of persistent nausea and vomiting. She stated that four days before, after having been on a picnic, she developed nausea and vomiting which had persisted for two or three days. The day before admission she had developed abdominal distention and dyspnea but had no pain.

She had suffered three previous attacks of abdominal discomfort and distention associated with nausea and vomiting and lasting for several hours. She also had a history of fatty-food intolerance. She was known to have had a large hiatus hernia for at least 12 years.

At the time of admission she was acutely ill with abdominal distention and nausea although without pain. She was a poorly nourished and feeble old lady. The general examination showed asthmatic rales in both lung fields. The abdomen was acutely distended and moderately tender. There were no abdominal masses; rectal and pelvic examinations were normal. The blood urea was 104 mg%.

On intravenous fluids and supportive therapy she improved markedly, and on the fourth hospital day, an upper gastrointestinal study showed that the barium entered the fundus easily but did not pass beyond until an hour later, when a small amount of barium was seen in the body of the stomach. The upper portion of the stomach was twisted upon itself so that the antrum was found in the chest at the proximal fundus and the duodenum and cardia remained in the abdomen.

Surgery was carried out through a left thoracotomy. The large herniated stomach was reduced and derotated, relieving the obstruction, and the hiatus hernia was repaired. The patient made an uneventful postoperative recovery.

Summary

Volvulus of the stomach is an acute surgical emergency which occurs with sufficient frequency so that it should be kept in mind by all physicians who treat abdominal disease.

The diagnostic triad is circumscribed upper abdominal pain with distention of the epigastrium and left hypochondrium; unsuccessful attempts to vomit; and inability to pass a gastric tube.

In doubtful cases X rays are often useful in making the diagnosis. Prompt diagnosis and surgical treatment are indicated.

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WHAT'S YOUR DIAGNOSIS?

A two-and-a-half-year-old boy had had a mild cold for several days that had become slightly worse the day before he was first seen. The temperature had suddenly risen to 104 degrees. His cough increased; he was grunting; there was a marked tachycardia. The breath sounds posteriorly were slightly suppressed. The abdomen appeared large; but the mother claimed that it had always been rather large.

He was given penicillin and admitted to the hospital later that day. The white count was 4,000 with slight neutrophilia. X-ray of the chest showed the diaphragm very high, and the base of the lungs appeared to be compressed. A flat plate of the abdomen revealed some distended loops of small intestine and, except for a small area, there seemed to be no air in the colon.

On the following morning the abdomen was more distended. The child held himself stiff and there was a questionable nuchal rigidity. Elevation of the alae nasi was very marked.

A consulting surgeon suggested waiting and in the meantime using gastric and duodenal suction, intravenous fluids, penicillin and aureomycin. On the following day a flat film of the abdomen showed an increase in the intestinal distention. The temperature was 104.6. The abdomen became extremely tense. The repeated white count was 5,400 with 81 per cent polymorphonuclears. Urine showed 1 plus albumin, 25 to 30 casts per high-powered field.

Three days after admission to the hospital the respiratory distress became acute and the intestinal loops were markedly distended with air. He was then taken to the operating room and a laparotomy was done.

What's Your Diagnosis? Turn to page 999.

Sensitive beings are not sensible beings. — *Balzac*

Sclerosing Neuroma as A Cause of Meralgia Paresthetica

Another example of "Nerve Entrapment Syndrome."

THE SYNDROME, meralgia paresthetica, has been known for more than 80 years.[1,2] The term is derived from the Greek words "algos" meaning pain and "meros" meaning thigh. The syndrome is characterized by pain, numbness, tingling, burning, coldness, or itching limited to the distribution of the lateral femoral cutaneous nerve of the thigh. This area includes the anterolateral portion of the thigh extending from just below the inguinal ligament to the upper border of the patella. Symptoms also may be felt as smaller, more circumscribed areas within the larger area. Symptoms usually begin after the age of 20 years and then may disappear spontaneously or may progress in severity until the patient becomes incapacitated.

Numerous causes for this syndrome have been proposed.[3] It is now generally thought to be caused by pressure on the nerve at any point in its course before the bifurcation. Because of the nerve's superficial position and the potentially constricting fascial layers through which it must pass near the anterior superior iliac spine, this area is most likely to be associated with the underlying pathology.

Anatomically the lateral femoral cutaneous nerve is an entirely sensory nerve, generally arising from the posterior roots of L-1, L-2, and L-3.[4] Passing behind or through the iliopsoas muscle, it courses inferolaterally on the deep surface of the iliacus muscle in the iliac fascia and enters the thigh just medial to the anterior superior iliac spine and below the lateral end of the inguinal ligament. It emerges from the fascia lata at a variable point up to 10 cm. below the anterior superior iliac spine. Just before or just after entering the subcutaneous tissues, the nerve usually divides into anterior and posterior branches. Considerable variation in this anatomic pattern has been described.[5]

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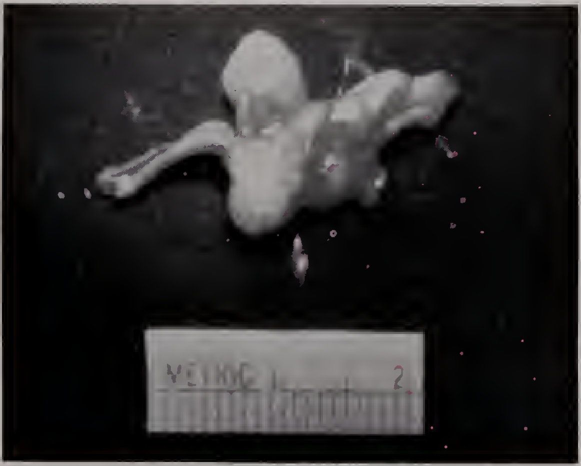

Fig. 2 — Surgical specimen.

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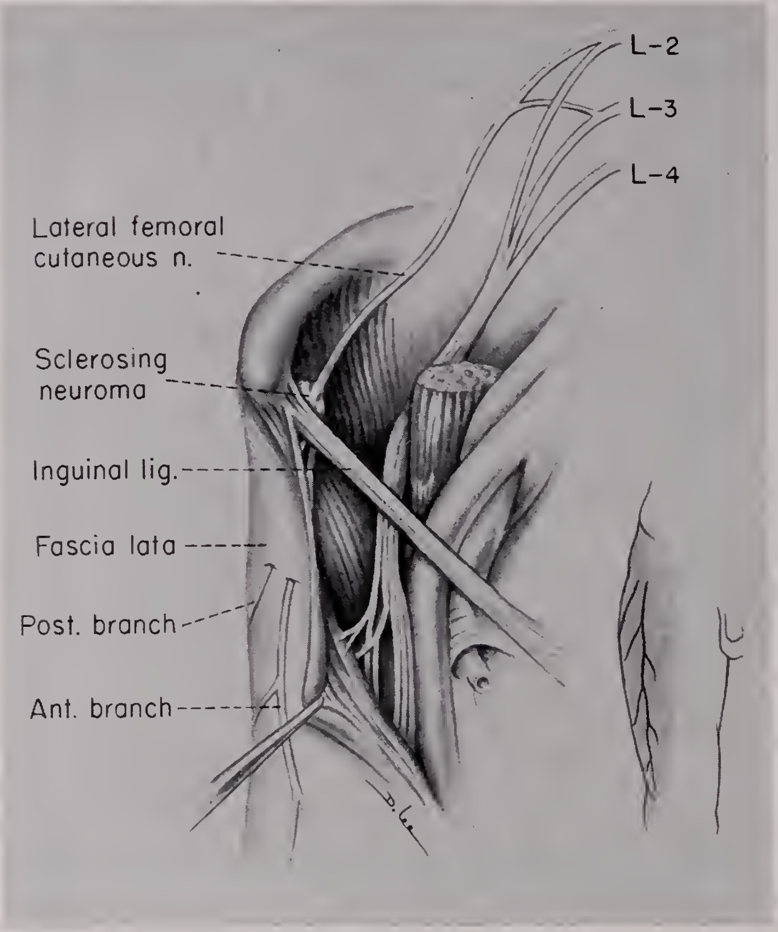

Fig. 1 — Drawing of operative site.

This paper reports a case of meralgia paresthetica caused by, or associated with, a sclerosing neuroma of the lateral femoral cutaneous nerve of the thigh.

Report of Case

The patient was a 56-year-old hospital employee who came to the Mayo Clinic complaining of pain in both hips and thighs. Approximately 20 years before he first had noticed occasional "numb, tingling, and pins-and-needles" sensations in the anterolateral part of his right thigh. More recently he had experienced occasional sharp stabs of pain and severe aching in the same region. These sensations were precipitated when he wore a belt, walked or stood for long periods, lifted heavy objects, sat in a bent or cramped position for prolonged periods, or when he pressed his finger just inside the anterior superior iliac spine. These sensations were temporarily relieved by local heat, massage, and ultrasound as well as by hot baths, meperidine, and bed rest. Ten days before he came to this clinic, the tingling and aching became constant for no apparent reason, and so severe that it interfered with sleep. For several years he had also noticed similar but not so severe sensations in the left thigh.

In addition, the patient complained of aching over both greater trochanters. This had been present intermittently for many years and, on one occasion, had been relieved for nine months by local hydrocortisone injection.

Physical examination showed only tenderness over both greater trochanters and hypoesthesia in the distribution of both lateral femoral cutaneous nerves. Roentgenograms of the lumbar part of the spinal column, pelvis, and hips were interpreted as normal.

Since the right thigh had been consistently more uncomfortable, he wished to have only that side operated on. Under local anesthesia an incision was made from the anterior iliac spine inferomedially for a distance of 5 cm. over the inguinal ligament. After the skin and subcutaneous tissues were reflected, the lateral femoral cutaneous nerve was seen (Fig. 1). The nerve was resected to include the mass (Fig. 2). The pathologic diagnosis was sclerosing neuroma; histologically the mass showed perineural fibrosis, intraneural fibrosis, and intraneural edema.

One week after operation the patient was free of symptoms in the right thigh.

Discussion

Nawratzki[6] observed a spindle-shaped swelling of the nerve adjacent to the anterior iliac spine and reported that microscopic changes in this swelling consisted of "perineuritis and interstitial neuritis." Others[7,8] have noted gross local nerve enlargement in this area but have not recorded histologic observations. We believe that meralgia paresthetica is another example of the "nerve entrapment" syndromes and that the tumor found at operation in our case represents the result of long-standing trauma or entrapment of a lateral femoral cutaneous nerve.

Summary

A patient with histologically proved sclerosing neuroma of the right femoral cutaneous nerve at the level of the anterior superior iliac spine associated with the symptoms of meralgia* paresthetica obtained complete relief of those symptoms after removal of the neuroma.

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*See Test Your Word Score Page 1029.

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ANSWER TO WHAT'S YOUR DIAGNOSIS

(from page 996)

A small amount of straw-colored fluid was found in the peritoneal cavity. The extremely distended small bowel loops were decompressed by suction with the needle. After the entire small bowel was delivered from the abdominal cavity, the cause of the obstruction was found to originate from a large cyst which filled the entire lower abdomen and the pelvis. This cyst could not be delivered until half of its contents had been aspirated. It contained grayish foul-smelling material and was found to arise from the transverse mesocolon. After dissection from its origin in the mesocolon, it was removed. Pathologic diagnosis: Infected lymphangioma.

After a stormy convalescence, the boy recovered.

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BRENNEMANN'S SYNDROME

(Abdominal Syndrome)

This is the abdominal manifestations of pain and cramps occasionally associated with acute or subacute rheumatic process in the child. This needs differentiation from acute mesenteric lymphadenitis.

The presence of C-reactive protein, an elevated sedimentation rate and antistreptolysin O titre strongly suggest rheumatic fever and should, therefore, aid in the diagnosis.

Durham — Encyclopedia of Medical Syndromes.

Drive Safely

There are two kinds of finishes you can put on an automobile — lacquer and liquor.

Lymphangiography

Study of lymphatics in clinical patients is a rapidly growing adjunct to diagnosis of hidden malignancies.

FOLLOWING THE work of Kinmonth,[5,6] interest was restimulated in attempts to visualize the lymphatic system. Further studies by Wallace[8] posed the question: how would lymphangiography help radiologic diagnosis and therapy in our department. The answer could only be obtained, if at all, by a series of cases with no restriction on presenting diagnosis. The arbitrary figure of 100 studies was selected; seventy-nine of them were of value and twenty-one were discarded due to technical problems. The method advocated by Wallace[8] has been followed, with modifications introduced to suit the local situation and apparatus involved.

Excellent analyses and descriptions of the lymphatic system have been produced in the recent literature.[2,4,7,8]

Technic

Initially a weak solution of Patent Blue V was injected intradermally into the dorsal webs of the toes or fingers. Later, a saturated solution was used with greater success. The amount injected is not important; if a small wheal is raised, as with a Mantoux test injection, satisfactory absorption is obtained. The skin lymphatics in young individuals will appear almost immediately; but with older patients multiple injections may be required.

The skin lymphatics usually lie over deeper channels. Using these channels as a guide, a longitudinal skin incision is made alongside a channel on the dorsum of the member and is elongated as required. The small blue lymphatic channel is elevated and cleared of all tissue. Usually the vessel goes into spasm, and milking of the channels distally will engorge the vessel. While visualizing the area with magnification the vessel is elevated and nicked with a pair of sharp scissors. A blunted 27 or even 25-gauge hypodermic needle with swedged-on polyethylene tubing is inserted into the channel. The blunting of the needle prevents perforation of the vessel. Five cc. of Ethiodal (38% iodinated poppyseed oil) in a 10-cc. syringe is attached to the tubing. A common retort stand with a clamp to hold the syringe and another ring clamp over the plunger to hold the graduated weights provide satisfactory, continuous flow. Usually the 5 cc. can be injected in one hour. Some extravasation is always present, but this should be disregarded and the injection

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A Local Evaluation

continued. Originally 15 cc. of Ethiodal was used, but this amount was gradually reduced to 5 cc. with a marked saving of time and with equally good visualization. Routinely, films have been obtained of the pelvis, abdomen, and chest at the end of the injection and at 24 hours. Extremity films have been obtained only if a block is suspected.

Material

Seventy-nine studies have been completed. These include the following: 36 lymphoma, 25 carcinoma, and 18 miscellaneous. Early studies have not been included due to technical difficulties — chiefly incompleteness due to inexperience. Twelve patients are now deceased; autopsies have been obtained and recorded in ten.

Results

Lymphoma

The lymph channels have a normal appearance unless there is a proximal obstruction, in which case the channels are distended. The lymph nodes absorb a part of the contrast material and have a lacy irregular pattern. The nodes show enlargement, particularly marked in lymphatic leukemia. If the node is totally involved with lymphoma, filling does

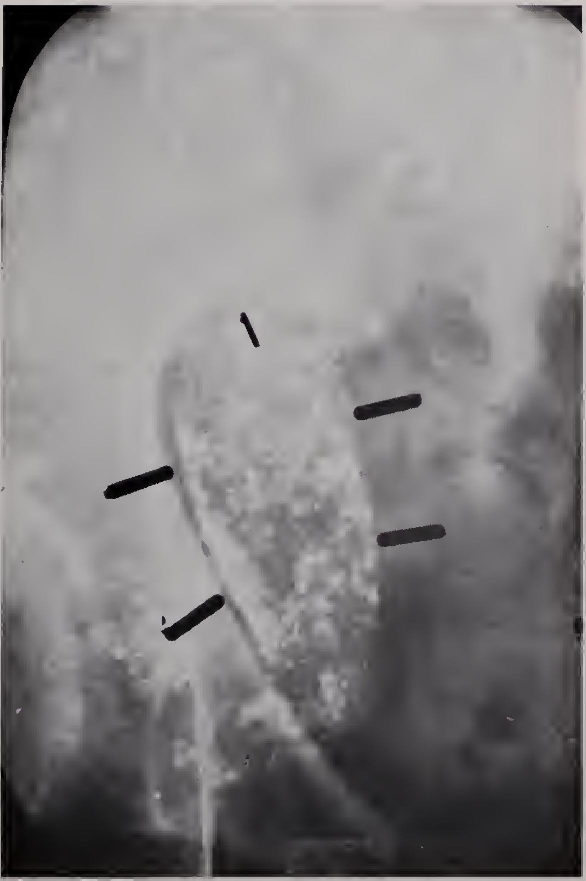

Fig. 1 — Male, aged 65, with chronic lymphatic leukemia. Note the lacy, irregular filling pattern of the enlarged node.

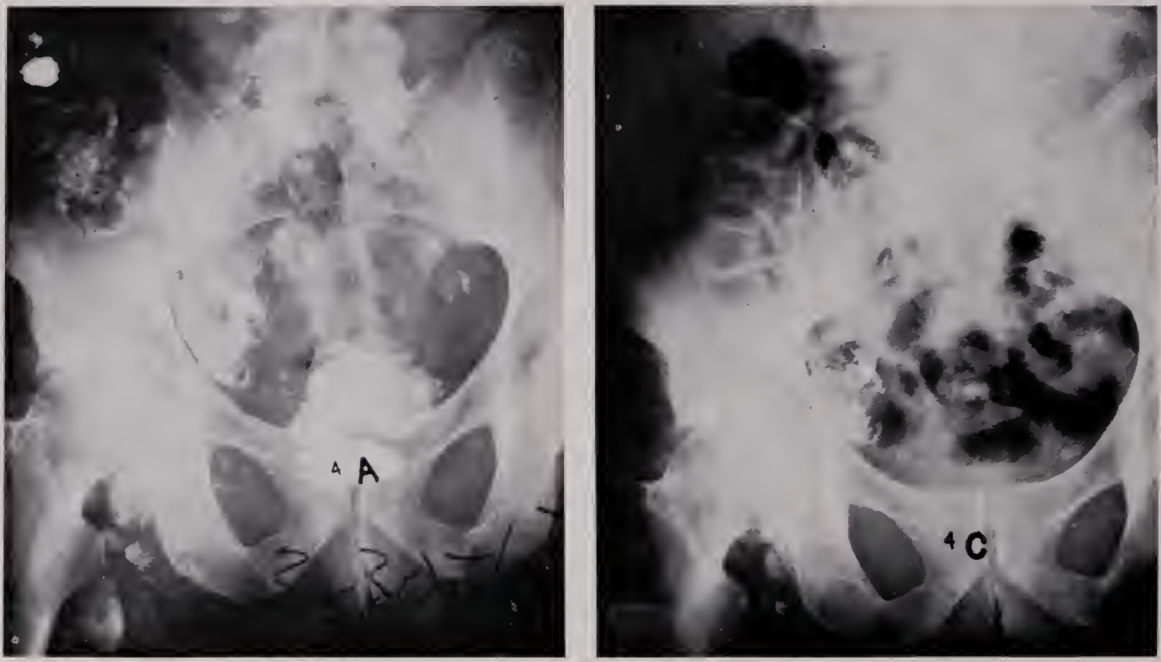

Fig. 2 *(left)* — Male, aged 50, with lymphosarcoma. In 3-30-63 the right femoral, inguinal, and iliac nodes have the typical enlarged feathery pattern. *(right)* Follow-up film 7-1-63 after radiation therapy — second injection demonstrates a marked decrease in the size of the nodes with least effect in the parailiac area.

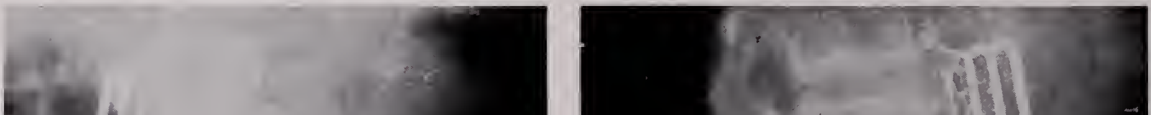

Fig. 3 — Male, aged 58, with carcinoma of colon. *(left)* The lymphatic channels are engorged and dilated to the level of the pelvic brim. *(right)* Proximally there is a block and the channels are fewer and deviated around several very large unopacified nodes. (A colostomy had previously been performed.)

not take place and a gap is left in the chain. The lymph channels may be deviated, indicating the presence of involved nodes (Figure 3).

Carcinoma

The metastases to the nodes are not visualized, but the nodal tissue takes up the contrast, giving a motheaten appearance. The afferent lymphatic channels may enlarge. Occasionally an increased number of channels and nodes may be visualized.

Lymphatic Obstruction

There must be great damage to the channels before lymphedema occurs. When a block to lymph flow is present, collateral lymph channels open and multiply, and bizarre patterns of drainage are demonstrated (Figure 4). Often the edema of the part is due to an obstructed vein; consequently venography should accompany or preferably precede a lymph-channel study.

Inflammation, retroperitoneal fibrosis, and

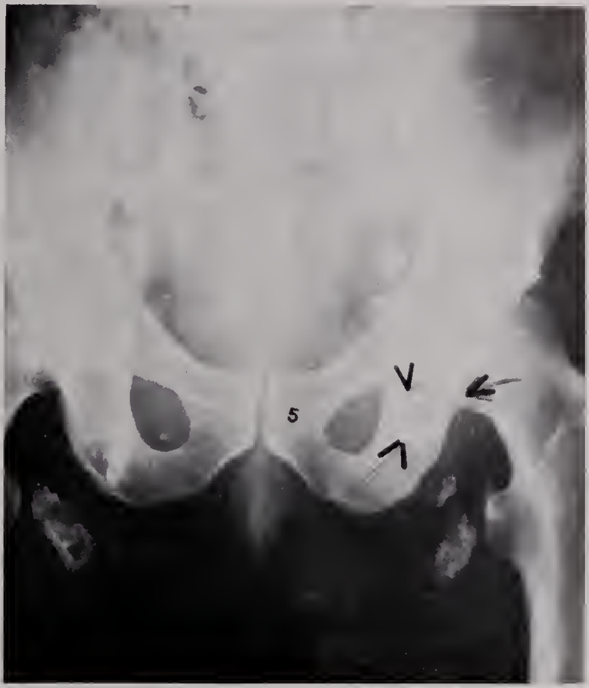

Fig. 4 — Male, aged 38, with carcinoma of urinary bladder. Nodes in left femoral area removed and sectioned. These contained carcinoma in the vaculated central area and normal lymph tissue at the periphery.

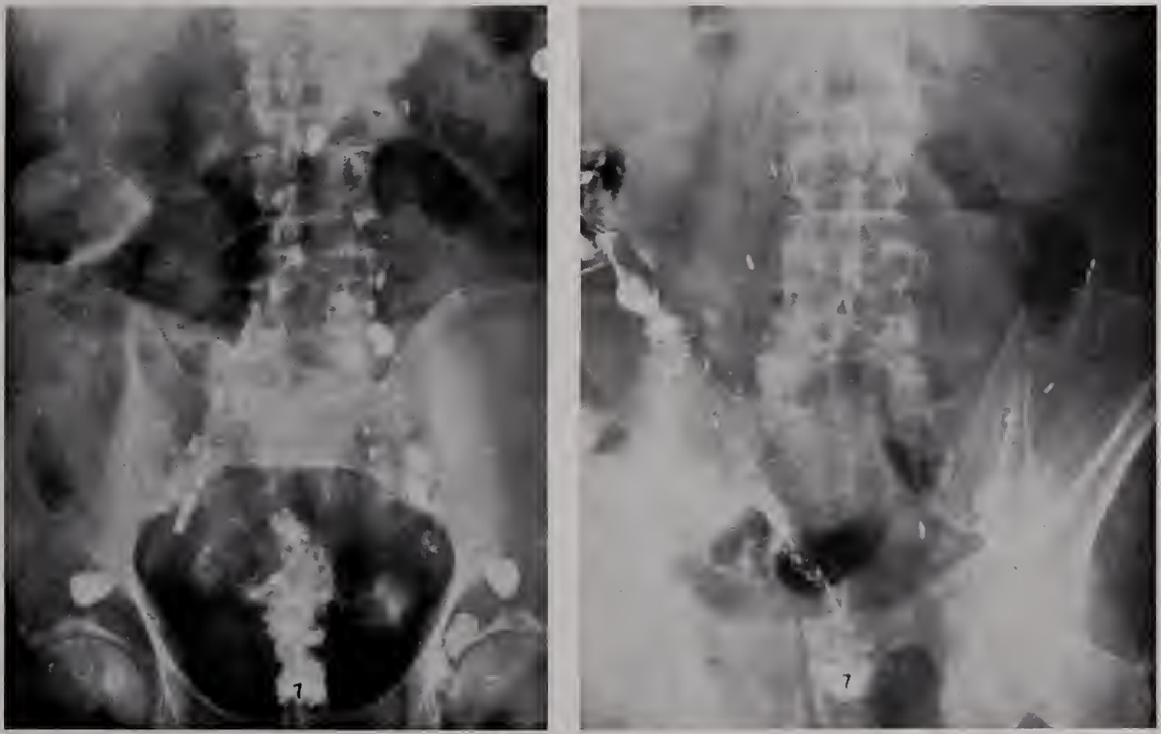

Fig. 5 — Male, aged 70, with carcinoma of rectosigmoid colon. *(left)* Preoperative film of lymphatic system — note involved nodes in parailiac and inguinal areas. By agreement the surgeons applied metallic clips in areas where nodes were removed. *(right)* Postoperative film obtained several months later (due to complications) discloses that the clips do not necessarily parallel the specified areas.

carcinoma situated elsewhere than in the pelvis show indeterminate results, in which the lymph nodes enlarge but show no characteristic pattern. The lymph channels may be decreased or increased but again without any determining pattern.

Use

Lymphangiography has proven to be of assistance in both radiologic diagnosis and therapy.

Diagnosis: (categories)

1. Suspicion — where there is an unproven but suspected diagnosis of lymphoma or carcinoma.
2. Location — to ascertain if disease is present in a certain location either initially or after treatment.
3. Extent — to determine location or diffuse involvement.

Therapy —

1. Radiation — as an aid in better localization, field size, sparing of normal structures, and determination of effectiveness.
2. Surgery — for better visualization and typing of nodes before, during, and after surgery.
3. Chemotherapy — for evaluation and follow-up.

Complication

A great deal has been written about oil embolism and lung involvement.[1,3,8] In all our cases no oil embolism and no lung abnormality were noted by impartial observers. No allergic manifestations of any kind were encountered. One wound infection occurred in a severely debilitated individual. Our good fortune may be due in part to the small series and/or to the small amount of contrast injected.

Isotopes

Iodine^{131}-tagged Ethiodal was injected and scanning procedures were attempted, but no definitive pattern could be obtained.

Radiation therapy with isotopes was not attempted, as it was concluded from pathological studies that the normal part of the node absorbed the contrast material and consequently would receive the most radiation, while the malignant portion absorbed little or none at all.

Conclusions

Lymphangiography is a relatively innocuous but tedious procedure.

Lymphomas yield the best positive results with carcinoma in the pelvic area running a poor second.

Lymphangiography provides a means of evaluating regional lymph-node status.

In radiation therapy, lymphangiography provides an aid as to type, duration and placement of therapy and is of special value in the follow-up of the patient.

Localization of nodes before, during, and after surgery has been developed.

When edema of an extremity occurs, a venogram should precede a lymphogram to determine the cause of blockage.

Isotopes have not been of benefit in either radiation diagnosis or therapy — in conjunction with lymphangiography.

Seventy-nine studies of the lymphatic system have been concluded for assessing the value of lymphangiography in a local large metropolitan hospital. It has been determined that lymphangiography is an aid in both radiation diagnosis and therapy in carefully selected cases.

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5-8 May be secured from the author or the reprints.

A man should choose with careful eye the thing to be remembered by.

— R. P. T. Coffin

Wheezing Infant[*]

- *Management*
- *of*

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ASTHMA IN infants presents some marked differences from the picture in adults. Some infants have the typical multiple musical expiratory rales, while others have a chronic cough with coarse, moist rales throughout the chest. During an acute attack of asthma these infants appear to be comfortable when lying down, whereas children will assume a sitting posture. The management of these infants is always a challenge. They may wheeze from inhalants, from foods, from infections, or from a combination of any of these factors; nevertheless most of them can be helped without elaborate workup.

Allergic Wheezing

Case Report

A child was born 11-10-60, the fourth to a mother with seasonal pollenosis. His formula was evaporated milk; fruit was fed him at two months and cereal at three months. At age four months he had some episodes of wheezing, coughing and questionable cyanosis. He did not appear acutely ill although he had sibilant rales throughout his chest. He was still wheezing a month later despite treatment with three per cent aqueous ephedrine, three drops every four to six hours. The mother was instructed to do individual feeding tests for wheat, oat, corn and milk — by omitting all forms of each food for four days and then feeding the omitted food on the fifth day.[1] The test with milk was positive. He was off milk and all milk products (most breadstuffs contain milk) until fourteen months of age when milk was reintroduced without causing symptoms. At the age of five he is eating everything but is rotating his diet, i.e., getting a different food of each food family each day. He represents the most benign type of wheezing infant, who makes a complete recovery without the help of a single skin test.

Skin Testing

When the asthmatic episodes are not controlled by dietary and environmental control, skin testing may be in order. Scratch tests for foods in infants are generally unrewarding, but several authors have stressed the prognostic significance of a positive scratch test to egg;[2] i.e., a poor prognosis for ultimate recovery. Intradermal tests for ragweed, alternaria, hormodendrum and house dust in an infant and subsequent hyposensitization are often indicated. When it is not feasible to do individual feeding tests, a provocative intradermal feeding test[3] is sometimes indicated for any food the child is ingesting, i.e., wheat, corn, egg, milk, soy and yeast. This test is made by injecting intradermally .05cc. of 1:5 dilution of the food in two sites on the upper arm, observing the child for ten minutes, and then injecting .02cc. of a 1:25 dilution intradermally and observing the patient ten more minutes. This test is probably 80% accurate.

Environmental allergens such as feathers are also important. In one dramatic case the cure came from getting rid of a feather puff which was a family heirloom.

Treatment

Drugs used in the management of asthma are used as in the older age group: sympathomimetics such as ephedrine and epinephrine; bronchial muscle relaxants such as aminophyllin, and expectorants such as potassium iodide.

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[*] Presented at the Fall Refresher Course of the American Academy of General Practice, September 16, 1964, in Minneapolis.

Asthmatic (capillary) Bronchitis

Asthmatic bronchitis begins as an upper respiratory infection. In a short time the infant develops rapid grunting respirations, a high fever and typical asthmatic rales throughout the chest. An X ray of the chest will usually be interpreted as showing a bronchopneumonia. Although the infant may be extremely toxic, the prognosis for recovery is good. Treatment consists of antibiotics, liquids and bronchodilators. Invariably there will be a family history of allergy; but not all of these children go on to develop true asthma.

Aspiration Pneumonitis

Aspiration pneumonitis may come from petroleum products either ingested or in the form of oily nose drops. In the case of ingestion of petroleum products such as kerosene, the question of the advisability of gastric lavage is unresolved. Most pediatricians feel that gastric lavage is not indicated.

Cystic Fibrosis

Cystic fibrosis is certainly the "bete noir" of anyone studying allergy, since the presenting symptom may be wheezing. The picture is complicated because some 15% of all cystic fibrosis patients also have allergic asthma. The diagnosis is confirmed by finding a high level of chlorides in the sweat, which may be collected by iontophoresis or by individual sweating in a plastic bag. (The latter procedure carries with it the very real risk of heat prostration and a fatal outcome.) Assay of the duodenal juice for trypsin is also diagnostic but technically more difficult than the above procedures. Both Shwachman's palmar sweat test and the assay of stool trypsin by digesting the gelatin of an X-ray plate fail to give a valid indication of the disease.

Case Report

This child was born normally, but during the neonatal period he developed signs of a bowel obstruction which was felt to be mechanical by the surgeon consulted. The X-ray department suggested the possibility of a meconium ileus. He recovered and did well until two months of age, at which time he had a choking spell while eating vegetables. Subsequently he had almost continuous difficulty with wheezing and loose stools. There was moderate improvement with dietary manipulation. At five months of age he was hospitalized; a palmar sweat test was normal and a chest X ray was not diagnostic. He was sent home but was readmitted to another hospital a few days later because of a recurrence of wheezing. He was started on antibiotics, but his condition deteriorated. A bronchoscopy showed no foreign body but did show an allergic-looking mucous membrane. At this time an iontophoresis was done, which showed the sweat chlorides to be 68 meq/liter. After a very stormy course, he expired. An autopsy confirmed the diagnosis.

This case emphasizes two points: first, that a normal palmar sweat test does not rule out cystic fibrosis and second, that any asthmatic infant who does not respond promptly to management should have the benefit of a sweat-chloride determination before an extensive allergic program is undertaken.

Cystic Fibrosis-Like Syndrome

There is another very definite syndrome: that of the fibrosis-like child who responds to the same management as that for cystic fibrosis, but in whom such a diagnosis cannot be made by the laboratory. Dr Warren Warwick[4] tells me that he had several of these youngsters in his cystic-fibrosis clinic at the University of Minnesota.

Case Report

A boy was born 2-12-63 and did well until 10-63 when he was admitted to St. Mary's Hospital with pneumonia and an interstitial pleural effusion. He was treated with antibiotics and made a slow recovery. Examination of the serum proteins by electrophoresis was normal; total protein was 7.6 mg. per cent with albumin 3.7 and globulin 3.9; an iontophoresis showed normal sweat chlorides. He went home on 10-23 and was readmitted 11-14 with another episode of pneumonia which was treated with antibiotics. Hospitalization lasted eight days. He remained well for five days and was again admitted for pneumonia. He was then hospitalized for ten days, during which time the diagnosis of allergy was entertained. He was sent home 12-7 on an elimination diet. He continued to cough and wheeze and was readmitted 2-15-64, at which time a barium swallow was normal. He was sent home 2-26 and readmitted 2-29 with bilateral otitis media. An X ray of the chest showed only a peribronchial infiltration. He had moderately coarse inspiratory rales throughout the chest, which were not typically asthmatic. A cine X ray of the esophagus, a screening test for gamma globulin, and a repeat sweat chloride were all normal. He was treated with antibiotics. The ears cleared, and he was then kept in a tent during naps and at night was given postural drainage as for cystic fibrosis. On 3-22 he was tested intradermally for ragweed, grass, house dust, alternaria, hormodendrum, cephalosporium and two mold mixtures, with negative results. In addition, provocative food tests were done for wheat, corn and milk with negative results. He has been kept on inhalations and postural drainage as for cystic fibrosis and so far has remained out of the hospital.

This patient wheezed, had repeated bouts of pneumonia, and has responded to cystic fibrosis management but does not have the laboratory findings of the disease.

Lobar Emphysema

Lobar emphysema is characterized by emphysematous expansion of one lobe so that dyspnea and cyanosis are produced. These symptoms may progress slowly or extremely rapidly until serious respiratory difficulty develops. One lobe, usually the upper, less often the middle and rarely a lower, is involved. Spells of dyspnea and cyanosis usually are the first symptoms. Wheezing respiration is not infrequent. On physical examination there will be an area of hyper-resonance with air entry diminished over the affected lobe. X ray will show the affected lobe to be translucent with adjacent lobes compressed or atelectatic. The heart is shifted away from the lesion. Treatment is lobectomy, although Korngold and Baker[5] temporized in two cases by performing lung punctures and withdrawing 200-300 cc. of air. This was followed by pneumothorax which cleared after thorancentesis. These are the only two cases in the literature cured in this manner. Leape and Longino[6] decry the use of lung puncture and feel the only valid treatment is lobectomy.

Extrinsic Causes of Wheezing

Extrabronchial pressure due to enlarged hilar nodes from tumor or tuberculosis may cause wheezing respiration. The treatment is the care and cure of the underlying disease.

Foreign bodies may be opaque or nonopaque. In my experience the most common nonopaque foreign body is a carrot, although the first foreign body I ever saw in a private patient was the cartilage from a chicken "drum stick" in a nine-month-old infant.

Congenital Abnormalities

Vascular Anomalies

Compression of the trachea and bronchi by vascular anomalies may cause wheezing in infants. The development of the aortic arch is effected by a complicated evolution of the primitive paired aortic arches. The symptoms depend on the location of the aberrant vessels and the degree to which they comprise the esophagus and trachea. Usually respiratory signs are more prominent than esophageal ones. Respirations are generally stridulous; but in many children expiratory wheezes, rather than inspiratory stridor, are heard. All signs may be agggravated by respiratory infections which are common in these babies. Severely affected babies lie with head extended, with flexion of the neck exaggerating the distress. Plain X rays may show the trachea with narrowing above the carina and displacement in either the horizontal or sagittal plane. Usually the most helpful X-ray sign is compression of the esophagus demonstrated with a barium swallow. Treatment is surgical.

Case Report

A boy, born 3-11-57, was well until two and a half weeks of age when the mother had to wean him because of lack of breast milk. He developed wheezing, which continued until 4-11, when he became cyanotic, was hospitalized and given ACTH. (His father had eczema and his mother had angioneurotic edema.) When there was no improvement with ACTH he was sent to Minneapolis. On physical examination his chest was full of inspiratory rales. An X ray showed a deep, rounded pressure defect posteriorly in the esophagus and a lesser indentation anteriorly at the same level. At surgery a double aortic arch was found; the anterior portion was divided. When last heard from in 1962 he was having no trouble.

Anomalous Left Pulmonary Artery

A fascinating variant of the above syndrome is a respiratory obstruction due to an anomalous course of the left pulmonary artery.[7] In the typical story, a newborn develops respiratory distress characterized by prolonged expiratory phase accompanied by wheezing. The right chest is hyper-resonant and breath sounds are decreased on this side. A chest film shows multilobar emphysema with a shift of mediastinum to the left. Later this mediastinal shift may disappear and emphysema becomes generalized. A barium swallow will show an anterior esophageal indentation near the level of the carina. On bronchogram the right mainstem bronchus will be constricted near its origin and the trachea deviated to the left.

This anomaly is characterized by an elongated pulmonary trunk following the course of the right pulmonary artery. A left pulmonary artery arises extrapericardially from this trunk. The left pulmonary artery lies anterior and superior to the right main-stem bronchus and posterior to the trachea. The right main-stem bronchus bears the brunt of the compressing force and the esophagus is compressed anteriorly.

Treatment consists of dividing the artery and rerouting it to its usual anterior position in relation to the trachea.

Tracheo-esophageal Fistula

A common anomaly familiar to most physicians is the syndrome of the usual tracheoesophageal fistula with cyanosis and choking after ingestion of food. One rare form of this syndrome is the H-type fistula with no esophageal atresia and a fistulous opening between the trachea and esophagus. Criteria for diagnosis are coughing, choking and cyanosis after ingesting fluids. There is no difficulty in swallowing; the distress occurs a few seconds later. Clear lung fields become full of coarse rales and rhonchi after swallowing. There are no symptoms after gavage* feeding. There is gastric distention after crying, straining and coughing. Confirmation of the diagnosis by X ray or esophagoscopy may be most difficult and cinefluorography has been most helpful. Treatment is surgical division of the fistula.

Cardiac Anomaly

A large left-to-right shunt from congenital cardiac disease may cause wheezing respiration. The diagnosis is usually obvious and treatment depends on the underlying cardial pathology.

Parasitic Disease

Visceral larva migrans[8] is rare in infants; it is usually seen in children older than a year of age and is manifested by leukocytosis, eosinophilia, hyperglobulinemia, hepatosplenomegaly and pulmonary infiltration. Diagnosis can be made with some certainty if there is a history of pica in a child who has a cat or dog, and with greater assurance by the finding of fertile toxocara ova in the soil or in the feces of the suspected animal.

The disease is caused by the ingestion of embryonated ova or dog or cat round worms, i.e., Toxocara canis or Toxocara mystax. Rashes of various kinds may appear. Pulmonary infiltration leading to respiratory distress, usually with wheezing, may be the most prominent manifestation or may even result in death. Treatment consists of antibiotics, steroids, and cautious trial of antihelminthics.

Summary

A wheezing infant is a diagnostic challenge. If there is a strong family history of allergy, allergic management may be tried. If there is not a prompt response, tests for cystic fibrosis should be carried out.

In infants with respiratory distress, a plain X-ray film may reveal emphysema in one lobe. In other infants a barium swallow may show esophageal compression due to vascular anomalies.

Foreign bodies either opaque or nonopaque to X ray may be suspected on the basis of history and on physical and X-ray findings.

Any child with repeated episodes of pneumonia associated with difficulty in swallowing or gastric distention after cough or straining should have the benefit of cinefluorography.

If there is pulmonary infiltration, eosinophilia, or hepatosplenomegaly in a toddler with pica who has a dog or cat, visceral larva migrans should be suspected.

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*See Test Your Word Score Page 1029.

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Character is what you are in the dark. — Dwight L. Moody

a Method of Measuring Psychiatric Diagnostic Skills

Physicians vary widely in their ability to successfully manage psychiatric problems. The authors present a method for screening medical students and young physicians for capabilities in psychiatric work.

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THE GROWING recognition of the problems of mental health in recent years has been paralleled by a growing recognition of the need to teach psychiatric knowledge, skills and attitudes to physicians. Psychiatric instruction has been increasing at both the undergraduate and graduate levels of medical training.

The University of Minnesota Medical School has in recent years greatly expanded its teaching programs in psychiatry, currently taught in all four years of medical school. The junior medical students have a ten-week exposure to inpatient psychiatry, and the senior medical students spend six months in the outpatient Psychiatric Clinic as part of their total clinic experience. The numbers of specialists in training in psychiatry at Minnesota has also greatly increased in recent years.

With this increased teaching activity has come the need to better understand and appraise methods and results of our various teaching programs. Both local and national research in appraising psychiatric teaching has become an important segment of investigation. Garetz and Magraw[1] are currently investigating changes in attitudes in medical students as a result of six months' intensive experience in Psychiatric Clinic. Stoller and Geertsma[2,3] have produced a sound motion picture of a psychiatric interview which they found to be a useful vehicle in testing psychiatric skills. Salzman and Goldstein[4] have used taped recordings to measure psychiatric skill.

The research reported in this paper was an attempt to use the method of Stoller and Geertsma to construct a test of clinical psy-

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The authors wish to express their sincere appreciation to the many individuals who, as consultants, advisors and subjects, made this research possible.

chiatric skills that would be of use in a local setting. They filmed a psychiatric interview, and the film was then shown to the staff psychiatrists, who described the patient using a Q-sort method.* With the staff Q-sort as a criterion they then tested various groups of subjects such as medical students in various years of training, college students, and psychiatric residents. They found that their method significantly differentiated groups at different levels of training and that the differentiation was in a direction that was predictable (i.e., skill increased with experience and training).

In order to apply this method in our setting, it was necessary to establish our own criterion, using staff people from our own department. When this was done, the film and Q-sort were used on medical students at various levels, social workers and psychiatric residents. Tables 1 and 2 summarize the data of this research.

Table 1 is a summary of data for four groups studied. Mean score represents the average score for that group and reflects the group deviance from the staff psychiatrists' criterion. The higher the score the less skilled the member of the group. Standard deviation represents the standard deviation of distribution of scores for the particular study group.

Table 2 shows the tests of significance when comparing the study groups, one with another. Table 2 indicates that there was a statistically significant difference between each group when compared with every other group — with the exception of the comparison between the psychiatric residents and social workers. The table further shows that the test result for each group is in the predicted direction in terms of the amount of experience of that group (i.e., staff psychiatrists show more skill than psychiatric residents, who show more skill than senior medical students, who show more skill than junior medical students).

TABLE 1

This is a summary of data for four groups studied. Mean score represents the average score for that group and reflects the group deviance from the staff psychiatrists' criterion. The higher the score the less skilled the member of the group. Standard deviation represents the standard deviation of distribution of scores for the particular study group.

Study Group	Mean Score	Standard Deviation
Staff Social Workers	70.13	15.00
Psychiatric Residents	70.21	12.57
Senior Medical Students	82.36	19.27
Junior Medical Students	91.91	12.02

TABLE 2

This is a summary of tests of significance. Each study group was compared with each other group to determine if differences in mean score were statistically significant.

	Social Worker	Psychiatric Resident	Senior Medical Student	Junior Medical Student
Social Worker		$t = .01$ $p > .9$	$t = 2.35$ $p < .02$	$t = 4.21$ $p < .001$
Psychiatric Resident			$t = 2.66$ $p < .02$	$t = 4.77$ $p < .001$
Senior Medical Student				$t = 2.67$ $p < .01$
Junior Medical Student				

The results of this research confirm the work of Stoller and Geertsma and point to the possible usefulness of the method in testing medical students and residents for their psychiatric diagnostic skill. This research also suggests the possibility of using this method and other similar methods to study the effectiveness of various psychiatric teaching methods.

Summary

A film of a psychiatric interview and a set of descriptive statements were used to establish a method of measuring psychiatric diagnostic skill in medical students and psychiatric residents. Skilled and experienced individuals performed better on this test than did less skilled and less experienced individuals. This method has promise as a technique of testing medical students and psychiatric residents as regards their psychiatric diagnostic skill.

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*Q-sort method is a method of quantifying descriptions. The subject is asked to sort a series of descriptive statements into usually seven to nine categories in terms of how characteristic the statement is of the subject being described. This method allows for quantification of the description and also quantitative comparison of descriptions of various individuals or groups.

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IT'S THE LAW

Blood Alcohol .15% Scientific Yardstick of Intoxication

A trial court was justified in concluding, upon all the evidence, that a driver had been proved guilty beyond a reasonable doubt of operating a car while under the influence of intoxicating liquor, a Connecticut intermediate appellate court ruled.

The driver was arrested when he was found slumped over in the front seat of a car either asleep or in a stupor. The car was in a stationary position in the middle of a parking lot obstructing traffic but its motor was running. The car had rolled out of a parking stall.

The officer aroused the driver after some difficulty and took him to the police station. The driver was unsteady on his feet, his breath smelled of alcohol, his eyes were blood-shot, and his speech was thick. He admitted that he had had several bottles of beer. The driver consented to a blood test which showed a blood-alcohol content of 0.16 per cent.

It is settled medical opinion that any person is unfit to drive when his blood-alcohol concentration is 0.15 per cent or more. The standards of the AMA, which are practical and fair, even generous, adequately served the purpose of providing a scientific yardstick of reasonable accuracy for evaluating the condition of a person accused of operating a car while under the influence of intoxicating liquor, the court said.

The car had to have been "operated" by somebody to get where it was found with the driver in it. There was sufficient circumstantial evidence to show that the driver had "operated" it while under the influence of intoxicating liquor, the court ruled. The driver's hips and buttocks were on the driver's side of the front seat. His head and the rest of his body were slumped horizontally on the front seat and generally to the right of the driver's side. His legs and feet were near, but not on, the controls, and the motor was running. It was practically, if not wholly, impossible to conceive that any other person could have gotten into the driver's seat, manipulated the gears and driven the car to the spot where it was found, with the driver sitting as he was with relation to the driver's seat and with his legs and feet situated as they were, the court said.

State of Connecticut v. Lariviere, 197 A.2d 529 (Conn., Aug. 26, 1963)

The Penalty of Overweight

A gross belly does not produce a refined mind.

What a man needs in gardening is a cast-iron back, with a hinge in it.
— Charles Dudley Warner

Radioiodine Serum-Albumin

Blood Volume Determinations

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HISTORICALLY, BLOOD volume measurement dates back to 1853 when Lehman and Weber studied two decapitated criminals by washing out their vessels to determine the volume.[1] This, of course, is a direct method. The indirect method on which all the current techniques are based should be credited to Valentin, who in 1838 suggested that with the infusion of a known volume of water into a living animal the circulatory volume could be estimated from the resulting dilution in accordance with the following equation:

$$\text{Concentration} = \frac{\text{Quantity}}{\text{Volume}}$$

and $Q_1 = Q_2$ because the solute does not change identity

therefore, $C_1 \times V_1 = C_2 \times V_2$

$$\text{thus, } V_2 = \frac{C_1 \times V_1}{C_2}$$

Blood Volume Measurement by Tracers

In order to furnish practical information, tracers had to be developed which met the following requirements and assumptions: First, a tracer should be nontoxic, nonantigenic, and preferably inert. Second, it should be easily identified quantitatively in small concentrations. Third, its quality or volume should not appreciably affect the volume of the blood. Finally, there should be no appreciable loss of the tracer during the time required for complete mixing.

Many tracers have been utilized satisfactorily, although none meets all the above criteria perfectly. They can be separated, however, depending upon their compartmental distribution into plasma volume tracers and red-cell volume tracers.

Red-Cell Labeling

The first practical approach to red-cell labeling was by Grehant and Quinquand in 1882, when they measured the cell volume with carbon monoxide.[2] Its absorption by pigments other than hemoglobin, however, rendered the method inaccurate. The techniques which utilize radioactive labeling of the red cells with Fe_{59}, Fe_{55}, P_{32}, and Cr_{51} are all accurate. Because of its practicality Cr_{51} has been utilized most frequently. The disadvantages of cell labeling compared to plasma labeling lie in the necessity for preparation of the cells, which is time-consuming and

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In 250 Cardiac Patients Undergoing Open Heart Surgery*

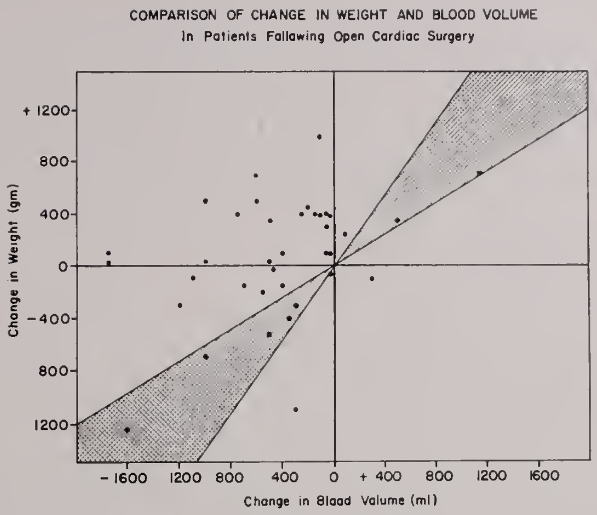

Fig. 1 — The blood volume change during operation as estimated from careful immediate pre and postoperative body weights in 38 patients was compared in the same patients to blood volume changes measured by RISA. Note that the two parameters agree in only eight instances (21%) even when a 40% range plus or minus is allowed (shaded area).

also introduces the possibilities of blood incompatibility or bacterial contamination.

Plasma Labeling

Plasma labeling utilizing dyes was initiated by Keith's use of vital red in 1915,[3] but did not reach practical popularity until the introduction by Dawson of Evans Blue (T-1824) in 1920.[4] The latter dye measures the plasma volume accurately. However, it may be unsatisfactory because hemolysis, free plasma hemoglobin, plasma turbidity, and repeated injections may interfere with the determination. The most commonly used and the most practical tag in our view has been radioiodinated human serum albumin. Seligman and Fine introduced the method of radioactive plasma labeling in 1943.[5] There are other plasma tags such as C_{14} and S_{35} which have been utilized experimentally with satisfactory results, but as yet their labeling processes are too complicated for clinical use.

The Problem

The problems posed by patients undergoing corrective cardiac surgery with extracorporeal circulation challenges the clinical judgment of the surgeon. Even with the most careful preparation, these patients sometimes represent extreme examples of physiologically poor surgical candidates. The spectrum sometimes includes patients with well compensated defects and no permanent alterations, but more frequently patients with intractable heart failure involving permanent cardiac, pulmonary, renal, and hepatic damage.

Since the respiratory, circulatory, nutritional, and excretional functions depend on adequate circulation, it is very important to know the effective blood volume available for tissue perfusion. This is particularly true for chronic illnesses with constantly changing cardiac outputs and wide volumetric alterations.

Expanded Blood Volume

Cardiac patients are in a precarious state, many having an expanded blood volume. Their poor myocardial reserve is aggravated by increased circulating catecholamines and adrenal hormones, which may not be restored to normal even after intensive medical therapy. In recent studies we have found that the preoperative levels of catecholamines are elevated in all patients with acquired heart disease in functional Class III and IV as well as in patients with congenital cyanotic heart disease.[6] Quick reflection on the physiologic responses to hypo and hypervolemia will indicate that these patients have already exhausted their first-line defenses, and even minor changes must mobilize a maximum response in order to restore homeostasis. Thus the patients' physiologic mechanisms usually require augmentation by the physician to preserve life.

Changes in Blood Volume

The weighing of these patients in the operating room before and after surgery was developed in order to allow an estimate of any changes in blood volume occurring during surgery.[7] This method was useful but proved to have many shortcomings. In 1959 we began to determine each patient's blood volume before and after surgery, utilizing dilution techniques with radioiodine-tagged human serum-albumin (RISA).

Methods

The patient is given a 4-ml. dose of radioiodine serum-albumin containing between 5 and 10 microcuries of activity after a blood sample has been drawn for background activity. An intravascular mixing period of 10 to 15 minutes is allowed and a final blood sample is drawn. A 4-cc. aliquot of each blood sample is placed in the scintillation well and counted for four minutes. The results are then compared to the previously counted standard dilution of the injected dose for that particular batch of radiodine-serum-albumin doses. The calculation is carried out as follows:

$$V_2 = \frac{C_1 \times V_1}{C_2}$$

$$V_2 = \frac{\text{Total Counts Injected - Background Counts}}{\dfrac{\text{Counts Final Sample - Patient Background}}{\text{cc. of Sample}}}$$

$$V_2 = \frac{2{,}800{,}000 \text{ Counts}}{\dfrac{2{,}800 \text{ Counts}}{4 \text{ cc.}}}$$

$$V_2 = 4{,}000 \text{ cc.}$$

Radioiodine serum-albumin's distribution and extent of dilution is taken to denote the total blood volume. The red-cell volume and plasma volume are then calculated from the hematocrit. The hematocrit, of course, is a large vessel value which can be further corrected to a total body hematocrit by multiplying it by approximately 0.91. (We do not make this correction.)[8]

In the 250 most recent cases analyzed, all patients had corrective procedures employing the pump oxygenator and a minimum of three blood volume determinations performed during their hospital stay. These were made initially a few days before surgery, immediately after surgery, in the post-anesthetic recovery room, and again on the first postoperative day.

At surgery the oxygenator was generally primed with 10% low molecular weight dextran 16-20 cc/kg. or with a dextran-mannitol combination. At the end of the corrective procedure and with the gradual return of good cardiac function, the contents of the helical reservoir were gradually pumped back into the patient.[9]

Results

Our patients were studied with carefully recorded weights immediately before and after surgery in the operating room, allowing for all the intravenous tubing, chest tubes and other paraphernalia. The weight change did not correlate well with the blood volume changes (Figure 1). From this data it may be seen that even if one allows a plus or minus 40% possibility in the weight-volume change correlation, only eight of our 38 patients showed a weight change correlating with the change in blood volume.

The preoperative blood volumes in the patients with congenital heart disease undergoing surgery are summarized in Figure 2. Figure 3 summarizes the comparable data for patients undergoing surgery for acquired cardiac disease.

The blood volume performed in the post-anesthetic recovery room usually indicated that the patient, in spite of very careful replacement of estimated blood losses, was 200-300 cc. behind his preoperative blood volume. The blood volume determinations on the first postoperative day showed almost no deviation from the preoperative values, thus confirming the inherent accuracy of the method when carefully performed.

Comments

The preoperative variation of blood volume in cc/kg. was fairly constant in those patients with both acquired and congenital disease, whether male or female. Thus the patient's lesion and/or sex did not appear to influence the blood volume as much as the cardiac disease. There appeared, however, to be some exceptions to this, in that we noted that patients with cyanotic type tetralogy of Fallot and those patients in the terminal phase from aortic or mitral valvular disease had the most elevated values. It should be emphasized that the blood volumes represented here were determined after intensive medical therapy, since they were done immediately before elective surgery.

The usual clinical formulas for estimating the effective blood volume have proved unsatisfactory in such patients. The utilizations of the height-weight formulas such as:[10]

PREDICTED BLOOD VOLUME

Men: $PBV = 0.3669 H^3$ plus $0.03219 W$ plus 0.6041
Women: $PBV = 0.3561 H^3$ plus $0.03308 W$ plus 0.1833

for blood volume estimation, seriously underestimate the blood volume in 70% of our patients. From all clinical indications these cardiac patients require their expanded blood in the early convalescent period. Thus our aim in the postoperative period was to restore the patient's volume to its preoperative levels, unless it was extremely high or unless central venous pressure was ominously elevated. Central venous pressure is certainly a valuable auxiliary tool in the postoperative management once the effective blood volume is known. But as the sole or prime determinant of volume, it may be grossly misleading, since the "normal" venous pressure for the cardiac patient may be several times the normal for noncardiacs.

One of the objections to the radioiodine-serum-albumin methods is that it fails to define the exact limits of the red-cell volume because of the shortcomings innate in hematocrit determinations. The other objection is that the distribution of radioiodine serum-albumin also includes a small portion of the extravascular compartment.[11] While conceding the theoretical validity of these objections from a practical standpoint, these errors are relatively small and are almost completely neutralized when a preoperative determination has been made, which is always possible in elective cases and nearly always possible in emergency situations, since the determination takes only 12 to 15 minutes.

Summary

Serial radioiodine serum-albumin blood volume determinations have proved reliable, accurate, and helpful in the management of over 1000 patients undergoing open cardiac surgery. Analysis of the data from 250 recent cases indicates that there is no substitution for this actual measurement.

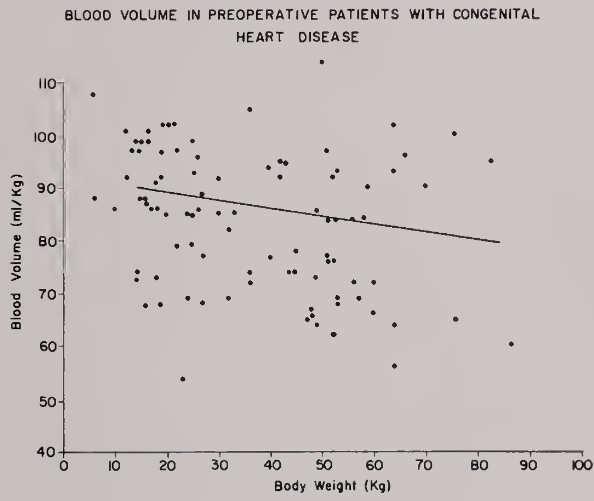

Figure 2

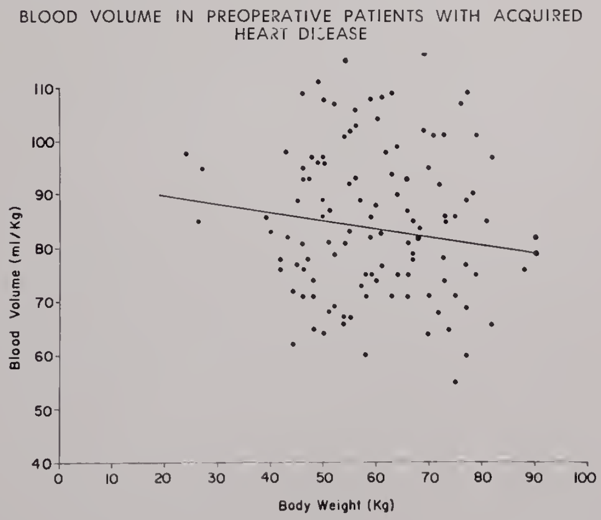

Figure 3

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August — Saint Roch

St. Roch (circa 1295-1327) is a noble and unforgettable figure among the saints whose commemoration dates fall in August. Historical facts about him are meager, but legend has immortalized him in a touching and heroic story of self sacrifice.

From his home in Montpelier, France, Roch set out as a young man on a pilgrimage to Rome. Journeying through northern Italy where the plague was devastating the entire area, he could not resist lingering there to care for the wretched victims, vast numbers of whom were dying either of the disease itself or of starvation before they could recover, as food, water, and nursing service became ever scarcer.

Shortly before Roch's arrival at Piacenza a small, persistent dog had attached himself to the pilgrim. During the height of the scourge, when Roch found it impossible to leave his sickest patients long enough to go out for food, the little dog Tino went instead. He had been trained to proceed to the shop of the one baker still operating on short rations in the town to pick up a small or even just a partial loaf of bread each day for his master to feed bit by bit to his numerous convalescent patients.

One day while returning to his roofless hut after his long day's ministrations, Roch himself suddenly succumbed, and, being unable to walk further, crawled into an abandoned shed on a hillside, where days later his little dog found him and saved him from imminent death by presenting him with a tiny loaf of fresh bread which he had coaxed from the baker, who later followed to the rescue.

Surely Tino's devotion to his master makes him almost as equally worthy on canonization as Roch himself; but being just a dog, he can receive only honorable mention in the annals of heroism. However, Roch and Tino are too inseparably linked for us to think of one without the other; and perhaps reflected glory shines all the more brightly.

St. Roch is also known as Roche, Rock, and Roque. His date is August 16.

Advice

"Be yourself!" is about the worst advice you can give some people.

— John Masefield

Severe, Recurrent Hypoglycemia

Due to

Chlorpropamide Therapy*

EVERETT H. KARON, M.D.**
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CHLORPROPAMIDE (DIABENESE), because of its biochemical properties, may cause severe, prolonged or occasionally recurrent hypoglycemia. Despite this possibility, only four such cases have been reported in detail in the English literature to date.[1-4] We should like to present another case and to discuss the possible mechanisms responsible for this potentially serious complication of oral hypoglycemic drug administration.

Case Report

The patient, a 40-year-old female, was first seen by one of the authors in March 1963. Her presenting complaint was referable to a recent knee injury; however, she also had noted ease of fatiguability and a 15-pound weight loss over the preceding six-month period. A routine urinalysis showed 4-plus glycosuria, and a fasting blood glucose was found to be 204 mg.%. She was started on an 1800-calorie diabetic diet and on chlorpropamide, 500 mg. each morning before breakfast. Over the next 10 days the blood sugar was gradually reduced to 109 mg.% and she regained three pounds of weight.

She was seen twice in the ensuing eight months and felt quite well. Her weight remained stable and urine-sugar tests were either negative or showed only a trace of glucose. Blood-sugar determinations were not obtained during this interval.

The evening of December 5, 1963, the patient reported intermittent numbness of the left side of her tongue and of the left hand of 12 hours' duration. Arrangements were made for her to be seen the next day. About two hours later, she again communicated with one of the authors, complaining of swelling of the left upper lip and some difficulty with her speech. She was advised to come to the hospital emergency room for evaluation at that time; however, she did not appear. The following morning, she was found to be unresponsive and was brought to the hospital emergency room.

Physical Findings

Preliminary examination revealed her to be semistuporous. Vital signs were normal. The skin was cool but not clammy. The pupils were equal in size and reacted normally to light. The eyeballs were firm. Her eyes exhibited a tendency to wander and she was unable to focus on a stationary object. Toe signs (Babinski) were positive bilaterally. The remainder of the examination revealed no abnormalities.

Response to Treatment

Blood for serum glucose determination was drawn immediately and 50 ml. of 50% dextrose solution was given intravenously. After administration of the first 40 ml., the patient became alert and coherent. It was then learned that she did not recall the previous evenings' conversations and therefore had not come to the hospital sooner. She did recall feeling hungry and said she had consumed four bananas, six English muffins and a quart of orange juice during the preceding night. This amounts to approximately 250 grams of carbohydrate. For two weeks prior to admission she had been aware of periods of extreme hunger and a craving for sweets. One week earlier, she had also experienced a disulfiram*-like reaction after ingesting a small quantity of alcohol.

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*Read before The Minnesota Society of Internal Medicine, May 16, 1964.

**From the Department of Internal Medicine, The Charles T. Miller Hospital, St. Paul, Minnesota.

She was admitted to the hospital for further evaluation and was placed on her previous 1800-calorie diet. The initial blood-glucose level was reported as 35 mg.%. During the day, she continued to complain of intermittent, mild dizziness and a "funny feeling." A blood-glucose level an hour after the evening meal was found to be 56 mg.%, and accordingly, a generous bedtime snack was given. At 3:15 A.M., 18 hours after admission, the medical intern was called to see the patient who noted profuse sweating, shakiness and slurred speech. Another 50 ml. of 50% dextrose was administered intravenously; however, a blood glucose was not obtained. She responded promptly and four hours later the blood glucose was 99 mg.%.

No further hypoglycemic symptoms were noted throughout the remainder of her hospital stay. Subsequent fasting blood-glucose levels were 110 and 105 mg.%. To rule out the possibility of a functioning islet-cell adenoma, an intravenous Tolbutamide test was performed. The curve obtained was typical for diabetes mellitus alone.

The patient was discharged on dietary restriction, and oral hypoglycemic agents were discontinued. On December 23, 1963, her fasting blood-sugar level was 80 mg.%. On September 30, 1964, when last noted, her fasting blood sugar was still only 74 mg.% after she had been off chlorpropamide for over nine months.

Discussion

The previously reported cases of severe and prolonged hypoglycemia following chlorpropamide administration have shown many similarities to this case. In all, the duration of coma, relapse into a deep hypoglycemic state, or persistence of symptoms despite apparently adequate therapy was 24 hours or longer. The reported blood-glucose level was 35 mg.% or less in each of the cases, reaching a low of 8 mg.% in one case 24 hours after admission and early therapy.[1] Two of the patients had received an evening dose of chlorpropamide the day prior to the development of hypoglycemic coma.[1,2] One case was that of a nondiabetic male who had been given large doses of chlorpropamide (2 grams per day) for two days prior to developing a prolonged hypoglycemia.[3] He developed permanent personality and intellectual changes with an abnormal electroencephalogram. However, he exhibited laboratory evidence for chronic hepatic disease; and this fact plus the very high dosage of drug administered were probably responsible for the unfortunate outcome. The three diabetic patients had taken the drug for periods nine days to eight months before developing their difficulties. Their daily dosage was 250-500 mg. of chlorpropamide.

Side Effects of Chlorpropamide

Hypoglycemic symptoms have been reported by most authors working with this oral hypoglycemic agent. The symptoms have generally been of mild degree and respond to oral glucose administration. Upon reduction of the drug dose, such reactions tend to disappear. Other side-effects from chlorpropamide include gastrointestinal disturbances, transient neurologic symptoms (primarily ataxia), skin rashes, somnolence, muscle weakness, chest pain, disulfiram-like reactions to alcohol ingestion, agranulocytosis and cholestatic jaundice. These side-effects have been variably reported in 2-8% of patients taking the drug and are felt to be dose-related. Agranulocytosis and cholestatic jaundice, however, may be due to true drug idiosyncrasy.

Physiologic Properties

Severe and prolonged hypoglycemic reactions fortunately have been rare. They are probably due to the combination of inherent physiologic properties of chlorpropamide plus the variations of individual patient response. It is known that chlorpropamide is rapidly and completely absorbed from the intestinal tract over a two to four-hour period with the peak hypoglycemic response occurring in about 10 hours. The drug is bound to plasma proteins and is slowly excreted in the urine in a chemically unchanged form. Knauff et al. have shown the metabolic half-life to be about 35 hours compared with a four-hour half-life for tolbutamide.[5] Following 16 days of continuous administration, demonstrable serum levels of chlorpropamide may be found for an additional 20 days.[6,7] Johnson and associates have described a dual disappearance rate for chlorpropamide which has not been observed in excretion studies of the other sulfonylurea drugs.[8] In normal subjects studied, over 80% of the drug is excreted in a rapid initial phase having a metabolic half-life* of 32 hours. The remainder is slowly eliminated in a second phase having a half-life of approximately 16 days. In diabetic patients who have been on chlorpropamide therapy, the amount excreted in this latter phase may increase two or three-fold. Whether this is due to increased plasma-protein binding, drug storage, perhaps in the liver, or some other mechanism is not known.[9] The clinical significance of this finding has not been elucidated. Serum levels of chlorpropamide, following repeated doses of the drug, show a rapid, straight-line cumulative curve for several days before a plateau is reached.[7] By contrast, repeated doses of Tolbutamide cause a subtle stepwise increase in blood serum levels, and the peak levels clinically are generally lower than those seen with chlorpropamide.[10] As the degree of hypoglycemia attained is a function of serum concentration of the agent used, it can readily be seen why chlorpropamide is three to six times more potent than Tolbutamide on a dosage basis.

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*See Test Your Word Score Page 1029.

The Possible Mode of Action

Despite extensive metabolic studies there is not complete agreement regarding the mode of action of the sulfonylurea agents in lowering blood sugar. The suggested mechanisms of action include stimulation of insulin release from beta cells, a direct effect on liver-glycogen metabolism, increased glucose uptake by skeletal muscles and inactivation of insulinase. Release of free insulin to act physiologically on the liver-glycogen stores would seem to be the probable mode of action.

Knowing the biochemical properties of chlorpropamide, one can postulate one or more of the following mechanisms to explain the appearance of the severe degree of hypoglycemia following its use in therapeutic doses: (a) simple relative overdosage of a potent hypoglycemic agent, (b) effect of cumulative high serum levels of the drug due to delayed excretion or release of stored or bound drug, (c) possible inactivation of serum insulinase at high serum levels, or (d) a normal response to a potent hypoglycemic agent following amelioration or remission of a treated, mild diabetic state.

We feel that this latter mechanism was responsible in the case presented, as the patient shows no diabetic symptoms or stigmata after cessation of drug therapy for 10 months.

Summary

A case of prolonged and recurrent hypoglycemia secondary to chlorpropamide (Diabenese) therapy occurred in a 40-year-old female patient who had previously taken the drug in the same therapeutic dosage for eight months without untoward reactions. Such severe reactions are rare, but the case is presented to alert physicians on the advisability for continued and close observation of such a patient, should a severe degree of hypoglycemia be noted.

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*See Test Your Word Score Page 1029.

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The fingers must be educated, the thumb is born knowing. — *Chazal*

*Paleopathology II**

What do we know about the diseases that afflicted our early brothers on this planet? What have we learned from the skeletal remains of prehistoric man?

From pathological bone remnants found in caves paleopathologists have discovered that cave bears and Stone Age man shared some of the same diseases, mute but convincing evidence of the homogeneity of evolutionary organisms. Modern man's susceptibility and vulnerability as compared with his distant progenitors' are striking.

On the femur bones of Java man appear exostoses which, on the authority of the noted pathologist Virchow, significantly resemble those of modern man. Remains of Piltdown man show evidence of pathological alteration of the skull bones, with the characteristic thickening associated with acromegaly and Paget's disease. The bones of one Neanderthaler reveal a fracture of the proximal end of the left ulna. Stone Age man must have suffered numerous fractures during his strenuous existence — combatting the forces of nature, the assaults of wild animals, and the hostility of his own species. What he did about fractures is something of a mystery; however, since only three out of 18 observed fractures show poor healing, we can assume that he was probably adept at applying splints.

Other pathologies among Stone Age men, noted by paleopathologist Roy Moodie, were spondylitis deformans, scoliosis, hyperostoses, arthridites, ulcerations, atrophy, exostoses, and osteomata.

Aside from splints for fractures primitive bone surgery appears to have consisted chiefly of providing a convenient exit for the demons considered responsible for disease: particularly headache and insanity. Countless primitive skulls show evidence of trephining, a voluntary and probably sacramental surgical procedure in primitive medicine. Of 120 individuals disinterred from a French burial mound 40 (33⅓ per cent) showed trepanation of the skull, an indication that headache or pain was discouragingly prevalent among our progenitors.

Besides trepanning to exorcise disease demons cicatrization was also resorted to by early man. From the skulls involved this barbarous procedure consisted in scraping or cutting a T-shaped cicatrice on the cranium and then cauterizing it with boiling-hot oil. A less frequent and more drastic measure than trepanning, cicatrization must have been more effective in ousting demons, since no crania show evidence of a repetition, whereas some skulls show numerous trepanizations, compelling testimony of early man's physical endurance and the persistence of his symptoms.

Within the limited framework of primitive Homo's conception of his mysterious and menacing world his attitude toward and defense against accident and disease display a resourcefulness and rationale by no means to be ridiculed or denigrated by his modern descendants.

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*See Minnesota Med 48:908, 1965.

Astrology

Mars, hot and violent, producing effects consistent with its nature, causes the acute diseases such as angina, spinal meningitis, and backache; whereas to Saturn, cold and restrictive, the chronic diseases are attributed, such as high blood pressure, impaired circulation, or locomotorataxia.

During August Mars is evening star and Saturn morning star.

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Side effects are relatively uncommon but among those reported are gastrointestinal irritation, sedation, dizziness, cutaneous manifestations, restlessness and insomnia.

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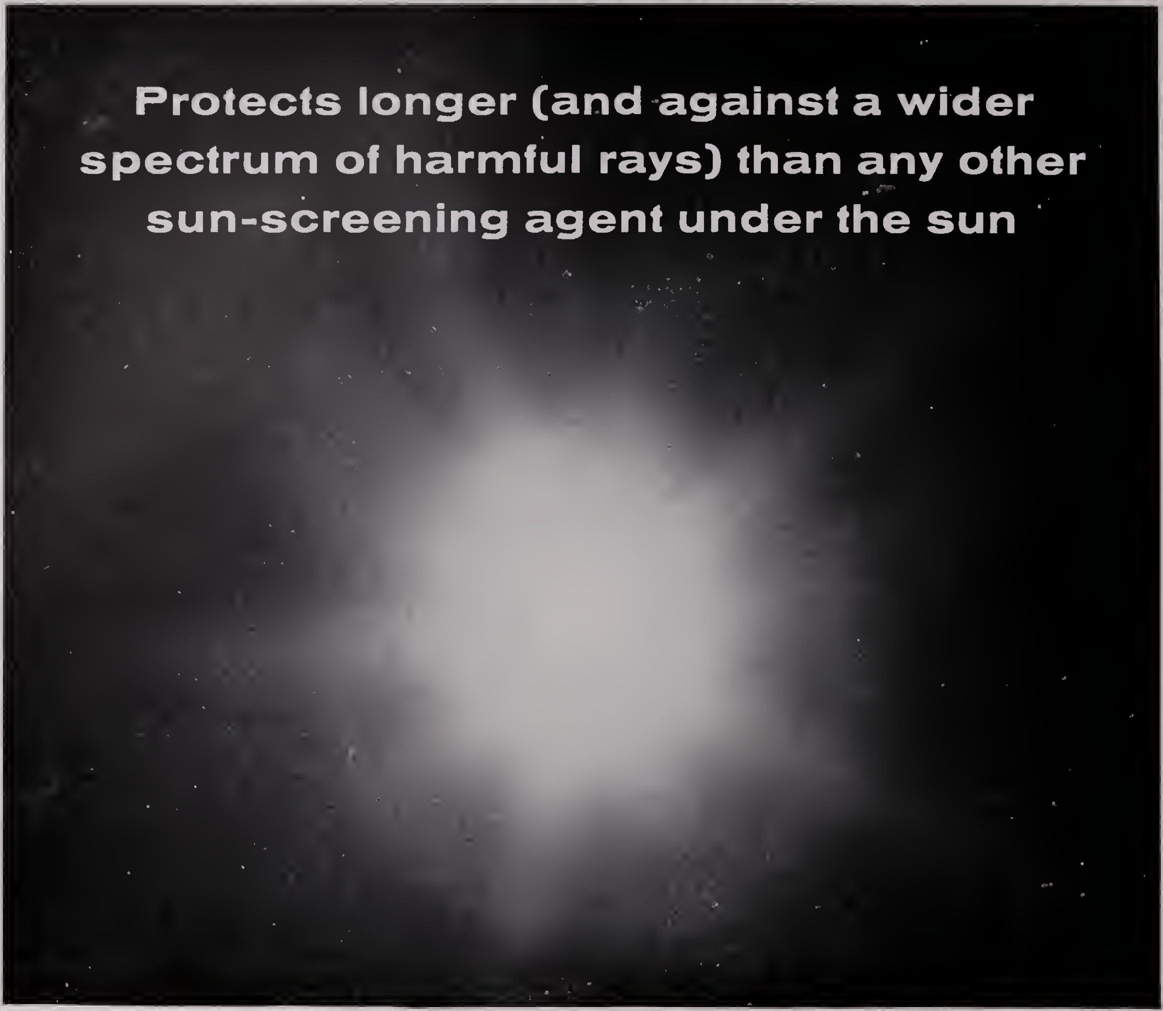
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Editorials

Concerning the Potassium Ion

In a June issue of Minnesota Medicine,* Snively and Westerman[1] emphasized the important role of the potassium ion in disease. This importance stems from the fact that potassium is an essential ion in numerous metabolic processes. As the principal intracellular cation it is necessary for the growth and repair of tissues. It is required for the synthesis of glycogen and appears to inhibit glycogen breakdown. By the generation of bioelectric potentials and formation of high energy phosphate bonds the potassium ion contributes to normal cardiac and neuromuscular function. The role of potassium in competing with hydrogen ion in the mechanisms concerned with the renal tubular reabsorption of sodium indicates the importance of the potassium ion in acid-base equilibrium. Moreover, potassium deficiency, even in the absence of metabolic alkalosis, is associated with a diminution in renal blood flow and glomerular filtration rate and with a pitressin-resistant defect in the renal tubular reabsorption of water. In view of the fact that all of these functional defects have their morphologic counterparts, as so well reviewed by Snively and Westerman,[1] the importance of understanding the pathophysiology of potassium deficiency by all who practice clinical medicine becomes readily apparent.

Numerous diseases and conditions which give rise to potassium depletion are summarized by Snively and Westerman.[1] In general, these may be categorized under the following three mechanisms: (1) decreased intake, (2) excessive gastrointestinal losses, (3) excessive renal losses. One might question the inclusion of the therapeutic low sodium diet, the nephrotic syndrome, and hepatic cirrhosis in this list. In those diseases in which sodium is virtually completely reabsorbed by the proximal renal tubule and renal excretion of sodium is negligible, sodium will not be available for distal renal tubular exchange for potassium; and potassium deficiency does not usually exist. Untreated congestive heart failure, decompensated hepatic cirrhosis, and the nephrotic syndrome are such diseases. Potassium diuresis may fail to occur even in the face of adrenocortical hyperfunction.[2]

For the diagnosis of a state of potassium depletion the history of a disease or a condition known to give rise to potassium deficiency is the most important single factor in diagnosis. The serum potassium concentration per se is frequently not a reliable guide to the presence or absence of potassium depletion because serum potassium levels may not accurately reflect cellular potassium concentration. Thus, in dehydrated patients the serum potassium may be elevated in the face of marked intracellular deficits of potassium. The experience with patients admitted with diabetic keto-acidosis is a classical example of this phenomenon. Prior to therapy the majority of patients with diabetic coma will demonstrate a serum potassium concentra-

Continued

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*See Minnesota Med 48:713, 1965.

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Contraindicated in comatose or greatly depressed states due to CNS depressants and in cases of existing blood dyscrasias, bone marrow depression and pre-existing liver damage. *Principal side effects,* usually dose-related, may include mild skin reaction, dry mouth, insomnia, fatigue, drowsiness, dizziness and neuromuscular (extrapyramidal) reactions. Muscular weakness, anorexia, rash, lactation and blurred vision may also be observed. Blood dyscrasias and jaundice have been extremely rare. Use with caution in patients with impaired cardiovascular systems.

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tion of 5-6 meq./L. Marked hypopotassemia may occur some 6 to 12 hours after insulin and parenteral fluid therapy have been initiated. Moreover, serum potassium is known to vary with the pH of blood — being high in metabolic acidosis and low in metabolic alkalosis. In patients with metabolic acidosis the shift of potassium from intracellular to extracellular fluid may maintain a normal or elevated serum potassium in spite of intracellular depletion of potassium.

A word of caution is indicated in two important aspects of the treatment of patients with potassium depletion. It is still not clear whether the functional changes of potassium deficiency are due to the loss of potassium intracellularly, to the secondary gain of sodium intracellularly, or to intracellular acidosis. There is, however, ample experimental evidence[3] indicating that high sodium intakes are lethal to potassium-depleted rats. This evidence, together with the fact that sodium may increase the urinary excretion of potassium, indicates that sodium-containing fluids should be given judiciously to the potassium-deficient patient. It is common for many clinicians to order parenteral saline and/or glucose solutions as initial fluid therapy. Solutions of glucose may also be associated with immediate deleterious effects in a patient with potassium depletion by accentuating the extracellular potassium deficit.

Finally, it may be noted that there are many problems to be solved in the understanding of this important ion. What is the mechanism of the functional and morphologic changes associated with potassium depletion? Does potassium deficiency lead to irreversible renal damage? Is the susceptibility to pyelonephritis increased? These and many more questions remain to be answered in the future.

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Pity the Unfortunate Patient with Hypertension Today

WITH THE gradual identification of secondary forms of hypertension, a profusion of diagnostic tests has resulted, for which each patient is a potential candidate. The excellent series of articles published in this journal mention only a few that have been developed with reference to the diagnosis of renal artery disease. Whole batteries of tests to exclude renal parenchymal, endocrine, or anatomic causes of blood-pressure elevation have also been developed in recent years. Many of these tests are time-consuming, uncomfortable, and rather expensive.

The better understanding of high blood pressure that these newer tests offer is valuable; but the vast majority of hypertensive patients have only essential hypertension. Therefore, it is particularly important that the physician originally evaluating the patient consider the severity of the blood-pressure elevation, the age of the patient, and any associated diseases before embarking on extensive diagnostic procedures. There is extreme need to carefully consider the real value of a given test to a patient and whether he, as an individual, will ultimately benefit from the procedure.

The ultimate object of these diagnostic tests is to determine the most satisfactory method of treating the patient. Although it is exciting to find increasing numbers of patients with renal arterial stenotic lesions, pheochromocytomas, or aldosterone-producing tumors, at the present time the physician should continue to approach the therapy of essential hypertension with the same zeal that he approaches the diagnosis of these rare secondary forms of hypertension.

Mahlon K. Burbank, M.D.*
Rochester, Minnesota

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There is general agreement that milder cases of osteoarthritis are preferably treated by simple analgesics. In many patients, however, this mode of therapy fails to give sufficient relief. Because steroids are not very effective in this form of arthritis, phenylbutazone affords the drug therapy most capable of relieving the more severe cases. For best results, it is recommended that treatment with phenylbutazone be combined with physiotherapy and other appropriate supportive measures.

Dosage
The initial daily dosage in adults is 300-600 mg. in divided daily doses. In most instances, 400 mg. daily is sufficient for maximum therapeutic response. A trial period of one week is adequate to determine the effects of the drug; if there is no improvement, discontinue the drug. When improvement does occur, dosage should be promptly decreased to the minimum effective level: this should not exceed 400 mg. daily, and is often achieved with only 100-200 mg. daily.

Precautions
Before prescribing, the physician should obtain a detailed history and perform a complete physical and laboratory examination, including a blood count. The patient should be kept under close supervision and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools. Regular blood counts should be made. The drug should be used with greater care in the elderly.

Warning: If coumarin-type anticoagulants are given simultaneously, the physician should watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea and sulfonamide-type agents and insulin. Patients receiving such concomitant therapy should be carefully observed for this effect.

Side effects
The most common side effects are nausea, edema and drug rash. Infrequently, agranulocytosis, generalized allergic reaction, stomatitis, salivary gland enlargement, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia are also possible side effects. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently.

Contraindications
These include: edema, hypertension, or danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. Because of the increased possibility of toxic reactions, the drug should not be given when the patient cannot be seen regularly, when the patient is senile, or when other potent chemotherapeutic agents are given concurrently. Large doses of Butazolidin® alka are contraindicated in patients with glaucoma.

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The Case for Cholecystostomy

PERHAPS NO clinical entity has been so obscured by folklore and half-hearted investigation as cholecystitis.

Descriptions of the histologic changes remain much as detailed by Aschoff. The exact sequence and nature of the tissue changes and disturbance of function are still not clear: hence a variety of controversial opinions about them. As a result, the treatment of the disease has been for the most part empirical.

We know that patients have gallstones and that as a result of foreign-body reaction with or without the interaction of pancreatic reflux and/or bacteria, inflammatory changes develop.

In a few instances acute cholecystitis results. This, if allowed to follow an uninterrupted course, usually results in a return to the status quo or in the so-called hydrops. In a few instances the gallbladder becomes gangrenous and ruptures. Bile peritonitis may result; but unlike the rupture of an appendix or other intraperitoneal appendages, suppurative peritonitis rarely follows.

The obvious procedure is to remove the gallbladder before this stage is reached. For numerous reasons this may be deemed inadvisable and, as an alternative, cholecystostomy is performed.

This prevents the liberation of bile into the peritoneal cavity but does little if anything to mitigate the disease of the gallbladder. Unfortunately, a certain number of patients die — not from gallbladder disease *per se* but because of the trauma of surgery and anesthesia or from some unrelated disease process.

If this number is large, as may be noted in the published series, the question naturally arises as to whether or not cholecystostomy is a reasonable procedure.

It is difficult to find a report of any considerable number of untreated cases of acute cholecystitis which have progressed to gangrene and rupture and have terminated fatally.

In contrast there are many published series of cholecystostomies which have an average mean mortality of 20%. Because of the many variables involved, the statistical material may not be conclusive; but the great disparity between the mortality of cholecystostomy and that of untreated acute cholecystitis contributes to the belief that with few exceptions cholecystostomy is an indefensible procedure. In short, if the mortality in acute cholecystitis cannot be kept within a 5% limit by cholecystostomy, other means should be employed.

Arthur A. Zierold, M.D.
Minneapolis, Minnesota

Collapsing Hip Nail*

THE REPORT by Dr. Harris* and his associates relating to the experience at the Hennepin County General Hospital (with the collapsing hip nail) emphasizes, and rightly so, *accurate reduction* in anatomic or slight valgus position, *locking* of the medial trabeculae of the femoral neck, and *compression* of the fracture site. The authors imply that their good results — and they are good results — may be due in part to the use of the Massie collapsing nail. Granting that a collapsing or telescoping nail is of no real advantage in intertrochanteric fractures, its use in intracapsular fractures has been discussed and debated in recent years. It has its proponents, and Dr. Harris and his associates appear to be of this group.

The sliding nail purportedly does not "hold the fracture apart" or allow migration of the nail through the head into the acetabulum. Actually, any flanged nail used in fixation of femoral neck fractures will tend to slide laterally and to protrude from the femoral cortex if and when absorption of the fracture site occurs, providing the nail is not fixed to the lateral cortex of the femur with

Continued

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*Harris, R. H., Mueller, G. F., Kiser, J. C., Peterson, F. A., Nydahl, M. J., and Hitchcock, C. R.: Collapsing Hip Nail, Minnesota Med 48:989, 1965.

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plate or screw. Thus, in subcapsular and transcervical fractures, the ordinary flanged nail, unfixed to the lateral cortex, "slides" by protruding from the lateral cortex, and allows the fracture ends to stay in apposition. There may be some advantage in the sliding nail in basilar fracture where one does fix the nail to the lateral cortex — providing that the nail truly does slide. The Massie nail, like other collapsing nails, is a mechanical device and sometimes does not perform in vivo as it is alleged to.

To prove whether the Massie collapsing nail is better than any other type of fixation would necessitate groups of patients treated comparably (except for the internal fixation device). It would be helpful if Dr. Harris and his associates had such a group or groups for controls.

Proper reduction, impaction, and co-operation of the patient postoperatively would seem to be the important factors in the healing of a fractured femoral neck. The type and method of internal fixation may not be so important. It has even been said that if reduction, impaction, and co-operation by the patient are satisfactory, fixation can be maintained with a "wet noodle." While this may be carrying the concept too far, it does make the point.

Mark B. Coventry, M.D.
Rochester, Minnesota

Test Your Word Score

Watch for the asterisks in the manuscripts each month and test your word sense!

Hypochondrial — *pertaining to area beneath the ribs* (page 994).

Meralgia — *pain in the thigh* (page 999).

Gavage — *feeding by stomach tube* (page 1008).

Disulfiram — *drug used in treatment of alcoholism* (page 1018).

Half-life — *the period in which radioactive substance disintegrates to half its value — variable from quadrillions of years to fraction of a second* (page 1019).

Schizoid mentation — *mental process or function resembling schizophrenia* (page 1049).

Megaloblastic anemia — *anemia with a large nucleated embryonic type cell, precursor of erythrocytes in an abnormal erythropoietic process, i.e., pernicious anemia* (page 1059).

Venenation — *poisoning* (page 1075).

O-o-o-p-s . . . We Erred!

The March, 1965 issue carried an editorial "'The Parnate-Specific Patient" by Burtrum C. Schiele, M.D. and in error, we listed Dr. Schiele's address as Smith Kline & French Laboratories.

Dr. Schiele is in no way associated with Smith Kline & French Laboratories. He is professor, Department of Psychiatry, University of Minnesota Hospitals, Minneapolis.

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Breast Cancer

BREAST CANCER arises from a primary focus in that organ in the great majority of instances. Ordinarily it begins as a small lesion. If it is less than one centimeter in diameter the incidence of metastases will be 40 per cent or less; sixty to 70 per cent of these small carcinomas will not have metastasized to the axilla. Five-year cure rates obtained in individuals without axillary metastases may be as high as 80 per cent. With axillary involvement even in highly selected series of cases this figure drops to 40 per cent and may be considerably lower.

The most skilled and experienced examining hand cannot identify the tiny tumor as benign or malignant with any degree of regularity or certainty. In the patient whose potential for cure is greatest the question of whether the suspected area differs from the surrounding breast tissue is often hard to answer. In any but the most superficially placed tumors the classical signs of breast cancer are the signs of well established disease. In actuality the earliest clinical manifestation of breast cancer is a minute and all but imperceptible change in consistency of a small area of the breast. Biopsy under these circumstances will often be negative; yet there is no other way to identify the small cancer most amenable to therapy.

A recent article in Minnesota Medicine* discussing radiographic breast examination stated that seven of 10 breast cancers can be diagnosed by clinical examination.* To accept this statement as a basis for practice renders a great disservice to women: it means that breast cancer is being neglected until there is an excellent chance that it is no longer confined to the breast. Attempts at cure under those circumstances by any therapeutic means or combination thereof is most likely to result in failure.

Confusion and contrary opinion may exist in the approach to the treatment of breast cancer; yet the inescapable fact remains that therapy directed toward the lesion which is still confined to the breast offers much. It is our duty as physicians to use the tools that we have — crude though they may be — in the most effective way. First and foremost among them is surgical biopsy of all suspicious areas in the breast.

The theory that biopsy should be carried out only when a "dominant" lump is identified allows many small cancers to become large. After such tumors have reached seven centimeters or more, axillary metastases alone are present in 80 per cent; tumors of such size are not infrequently seen in surgical practice today. Small wonder that a segment of lay opinion fears "cutting a cancer."

Physical examination of the breast is not easy. Normal variation is great. The large, dependent, mobile breast defies palpatory identification of small tumors deep in its substance. In these and other selected cases roentgenographic examination may be a helpful adjunct. New modalities may successfully probe the breast and refine our diagnostic skill. Any woman of reasonable intelligence, armed with proper knowledge, can learn to examine her breasts with accuracy in regard to early change. With concise instruction as to ovulatory function and periodic change secondary to hormonal ebb and flow, mystery and fear of the unknown can be replaced with knowledge. Frequently this will result in bringing breast tumors to the physician's attention at a time when they can readily be cured. It is appalling to note that on the average 10 months or more elapses from the time the patient is first aware of symptoms (usually a lump 80+%) before she presents for definitive treatment.

The efficacy of early identification of small breast cancers followed by prompt surgical treatment cannot be disputed. Let us not fail the woman who presents with an early change in the breast.

Until our imperfect understanding of this dreadful common illness improves, those trite words EARLY DIAGNOSIS constitute our most effective approach to this problem.

Daniel J. Moos, M.D.
Minneapolis, Minnesota

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*Cohen and Pick: Dominant Masses & Mammography. Minnesota Med 47:1449, 1964.

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Letter to the Editor:

Dr. Arnold Kremen* has done it again. The caduceus is *not* our "symbol of medicine," modern or otherwise, and it does *not* have "a serpent" wrapped around it. It is the emblem of the messenger god, Mercury, who inherited the functions of the Greek Hermes, who had in turn inherited the functions of the Babylonian messenger god, Ningishzida. The emblem of all three was and is a *pair* of snakes, intertwined in coitus, symbolic of the creation of new life in the springtime in response to the message borne to all living things by the sacred messenger. The caduceus had, and has, nothing to do with medicine.

The staff "wrapped" or entwined by a single serpent is the emblem not of Mercury but of Aesculapius or Asklepios, the Greek (and, by loan, Roman) god of medicine. This staff was a proper walking staff or cane — not a rod of office or scepter as in the case of Hermes and Mercury — so that the gold-headed cane, or any cane, is indeed appropriate to a physician.

Harry L. Arnold, Jr., M.D.
Honolulu

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*The Gold Headed Cane Tradition. Minnesota Med 48:63, 1965.

The Editor's Soliloquy

Eschew that Cliche

There is almost nothing more devastatingly disarming than the cliche: that hackneyed, stereotyped expression that somehow catches the fancy of the unthinking vulgus.

Eric Partridge, British authority, both raises and answers the question as to why cliches are so popular and so extensively used. He says: "An uncultured little-reading person sees a stock phrase and thinks it apt and smart." So it catches on!

Many cliches were originally vivid and striking linguistic *tours de force,* which by overuse became superannuated. As our American authority, H. L. Mencken, put it: "Many an apt and ingenious neologism, by falling too quickly into the gaping maw of the proletariat, is spoiled forthwith and forever."

Legion are those who believe they are injecting verve and vigor into their vernacuiar with a profuse spattering of such expletives as: "Says you!" "I'll tell the world!" "Alrightie!" "You can say that again!" Though these trite expressions make us wince a bit, we wryly accept them for their hearty buoyancy and artlessness.

Slightly more irritating is the pseudoscientific cliche with its aura of authority and irrefutability. This category includes the sympathy-compelling neomedical cliche which flows so officiously from the mouths of assorted hypochondriacs et al. and is calculated to endow its utterer with a halo of special dispensation for his strep throat, his slipped disc, his toxic bowel, his tired blood, or his whiplash injury. This individual's nerves are astonishingly volatile and versatile: they can be frayed, pinched, shot;

Continued

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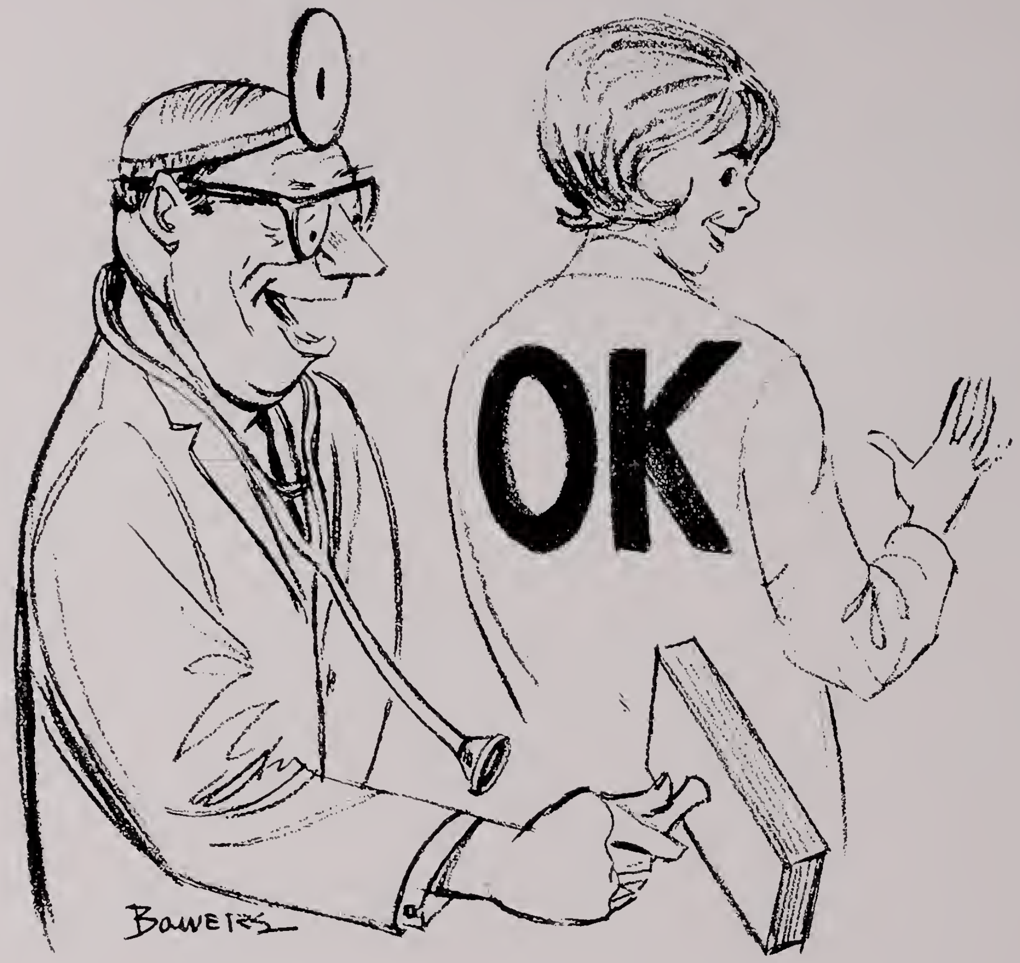

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or he can be a bundle of them! Whatever his distinctive lament, his ego is thereby vastly inflated.

Even more annoying is the individual with a flair for the foreign cliche, the unfamiliarity of which seems to deny its commonness and belie its platitudinousness — thereby setting up a snob appeal from which few dare demur. To the discomfiture of his listeners he embellishes his conversation with unexpected and startling *bete noirs* and *alfrescos.* Myriad are the atrociously mispronounced French and Italian terms that issue glibly from the mouths of the linguistically pretentious who wish to humble their peers and awe the unthinking masses who delight to sit in the shadow of the more sophisticated.

The category of personally-directed cliches covers a wide spectrum. At one end is the purely affectionate, back-slapping "You old son of a gun!" Next comes the disarming, chuckle-producing label designed to insinuate subtle contumely without incurring liability or arousing resentment: 'absent-minded' or 'long-haired professor,' 'pill-dispenser,' 'head-shrinker,' 'saw-bones,' etc. These slightly barbed sobriquets provide a convenient weapon for 'slaying' friend or foe alike with complete immunity from reprisal and are deliberately used by the invidious who wish to humiliate or derogate their superiors.

The snide term 'egghead' is employed by the secretly envious to disparage the individual with a high I.Q., who may have attained recognition for academic achievement, and who declines to look, act and sound plebian and scorns to adopt the mucker pose.

The reprehensible character-slashing cliche is that unsubstantiated but ex-cathedra announcement that so-and-so is an 'extremist,' an 'atheist,' a 'communist,' an 'anarchist,' or some other 'ist' — no less sinister and subversive. These are the most indefensible and unpardonable of the pejoratives, because they are too often fatally damaging to the reputation of the victim to whom they become attached.

The press and other news media are notorious for their exploitation of cliches, especially in the heat of political controversy or war hysteria. For example — when one's enemy makes a coup, military diction terms it a 'sneak attack'; but a coup achieved by one's own consecrated forces is a 'surprise attack,' or is even highly touted as a stroke of 'brilliant strategy.' Such stereotypes are avidly seized upon by the undiscriminating and gullible, to be perpetuated in the argot of headline history that shapes public opinion and so determines foreign policy.

Excepted and omitted from our repertoire are many immortal phrases: the March of Time, the Patience of Job, and the Sword of Damocles — which can be used indefinitely without losing luster and power; they are classics without which our language would be the poorer and meaner.

Whether condoned or condemned, however, cliches as a generality give us a "pain in the neck." Oops!

Carl O. Rice, M.D.

The Penalty of Overweight

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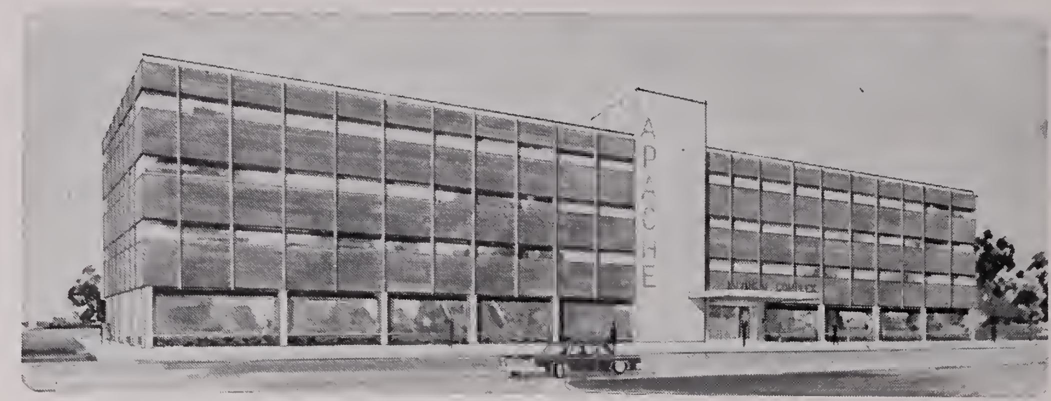
Cyril M. MacBryde, M.D., Signs & Symptoms, Lippincott Co.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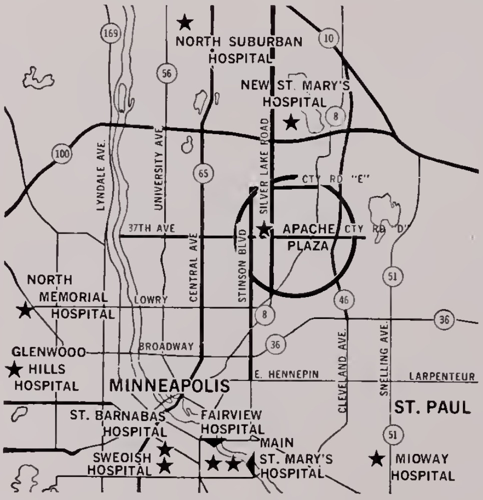
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QUESTION: Have any drugs been developed which actually afford protection against ionizing radiation?

ANSWER: Some experiments have shown that radiation damage may be mediated through radiation-produced decomposition of water within the tissues. However, an adverse effect on vital cell molecules results from these highly reactive decomposition products of water, a fact which suggests attainment of protection through development of a chemical agent that can "intercept" these breakdown products of water.

Anoxia has been observed to increase survival rates in experimental animals, suggesting the use of drugs which create tissue anoxia through a variety of mechanisms.

Following irradiation to a target molecule there can result loss of a hydrogen atom, with the formation of a radical on that molecule. This radical may react with oxygen to form peroxidases, to decompose, or to cross link with other molecules. Chemical agents which could serve as hydrogen donors, it is postulated, might neutralize these very reactive radicals.

Thiols have been found to be more sensitive to radiation than disulfides. There is hope, therefore, that the critical thiol group may be shielded by being bound in a mixed disulfide linkage with a protector molecule.

Some of the more promising agents tried to date include aminothiols and their disulfides (e.g., cysteine, cysteamine, mercaptoethylguanidine), amines (e.g., histamine), dithiocarbamates, cyanide and organic nitriles (e.g., potassium cyanide), and others (e.g., steroids).

Most of the promising work has been done on experimental animals. Results showing protection by a dose-reduction factor of 1.5 are common. Improvement in results is also being sought through use of a combination of drugs by which it is hoped that the therapeutic effects will be additive, while the toxic effects will not be.

Talking is a hydrant in the yard and writing is a faucet upstairs in the house. Opening the first takes all the pressure off the second. — Robert Frost

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You can't stop a leak in the water faucet by plugging the hole in the bucket. — COR

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Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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Fracture–Trauma Conference

—Trapped Fibula—

An Injury of the Ankle Which Requires Open Reduction of the Fibula

Many fractures and fracture dislocations occur in various parts of the skeletal system which are not reducible to their anatomical position because of soft tissue interposition or other unusual characteristics of the skeletal injury itself, such as the presence of intra-articular fragments. The posterior tibial tendon, peroneal tendons, ligamentous tissue and periosteum are examples of structures which are often found to prevent the anatomical reduction of skeletal injuries of the ankle.

There is an infrequent injury to the ankle which has not been widely reported and is often misdiagnosed and mistreated. Beware of this injury! It is one in which the proximal portion of the fibula has been displaced and trapped behind the posterolateral ridge of the tibia. This can occur in either a bimalleolar fracture-dislocation or subluxation of the ankle, or bimalleolar or trimalleolar fracture without a subluxation or dislocation. In some cases a subluxation or dislocation of the talus has occurred but is reduced by the patient or ambulance attendant by the time x-rays are taken and the physician sees the patient.

The mechanism for this injury is not clear. As the leg rotates upon the foot, the intact fibula may be pulled posteriorly behind the tibia by the lateral collateral ligaments and interosseous membrane. In the mechanism of this injury the talus is rotated posteriorly from under the tibia, causing further stress on the lateral collateral ligaments, which eventually leads to the fracture of the fibula against the posterior tibial border. The proximal fibular fracture thus becomes "locked" in this position.

It has not been definitely explained why the proximal fibular fragment becomes locked. Bosworth felt that it was held in this position by the tight stress of the interosseous membrane above the fracture site.[1] The author of this article has attempted to reproduce this injury in a number of cadavers. It is his opinion that there are three possible factors involved in maintaining the posterior displacement of the proximal fibula: (1) tight stress of the interosseous membrane; (2) entrapment into the interosseous membrane and/or other soft tissue structures at the posterior aspect of the tibia; (3) and the most important, the displacement of the proximal fragment anteromedially to the distal fragment so as to become locked by the distal fragment.

Case Report

The patient is a 17-year-old white female, who while walking her dog stepped off the

Continued

curbing, sustaining an injury to her right ankle. She was taken to the emergency room, where the house physician noted a deformity of the ankle, which represented either a subluxation or a dislocation of the ankle joint. In order to make the patient more comfortable while waiting for her private physician, he manipulated the ankle and reported that the deformity became reduced. Subsequent x-rays revealed a bimalleolar fracture of the ankle. She was taken to surgery and under general anesthesia her ankle was manipulated and placed in a plaster cast. Post-reduction x-rays left some doubt in the physician's mind as to his reduction. Further consultation was then obtained, the cast was removed and the ankle remanipulated. The second post-manipulation films revealed that the proximal fibular fragment had not changed its position (Fig. 1). Also noted was an unusual, double transverse fracture through the medial malleolus. The patient's ankle was then prepared for open reduction. A posterolateral skin incision was made over the fractured fibula, and the proximal fibular shaft was found to be locked in back of the posterolateral ridge of the tibia. A pereosteal elevator was placed over the anterior aspect of the shaft of the fibula and by considerable pressure applied posteromedially and then laterally; the fibular shaft was freed and the two fragments fell into an anatomical position. A biocortical screw was then placed across the fractured fragments. Attention was next directed toward the medial malleolus fracture; two Kirschner wires were placed across the fracture fragments (Fig. 2-a, 2-b). The patient has been followed routinely since surgery and has made satisfactory progress.

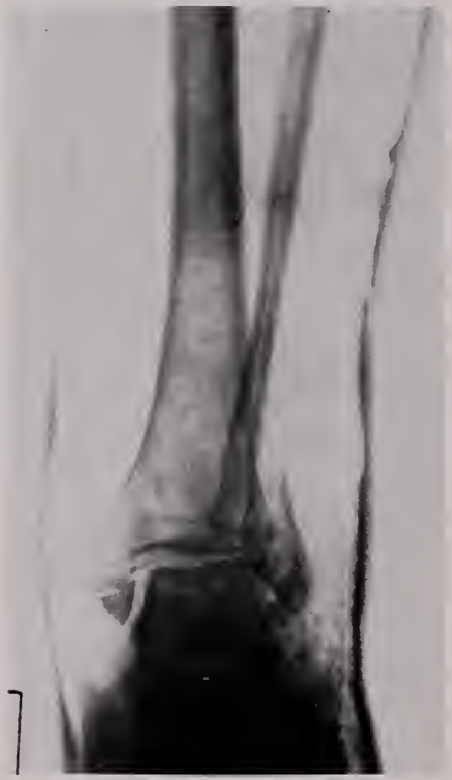

Figure 1

Discussion

This injury will become more apparent after an attempt at closed reduction is made and post-reduction films show that the position of the proximal fibula has not been changed. Do not be misled into believing that the x-rays taken were not truly anteroposterior or lateral views. On the anteroposterior view the proximal fibula can be readily seen to be displaced posteriorly and medially (Fig. 1). This will be confirmed on a lateral x-ray.

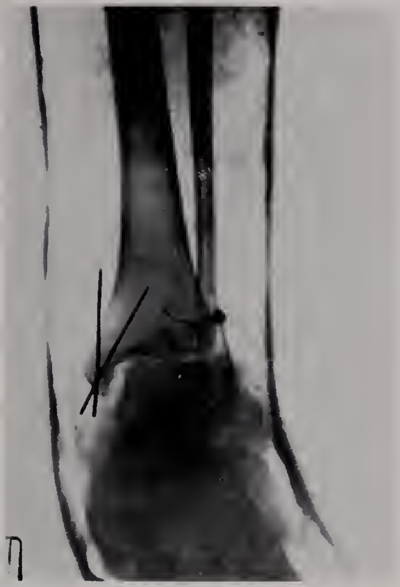

Fig. 2-a

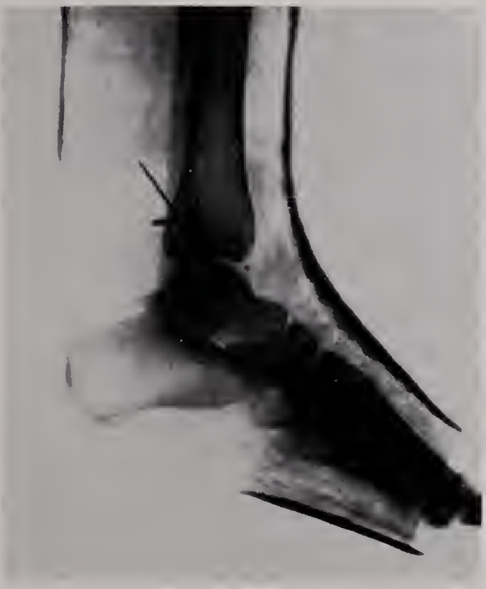

Fig. 2-b

The treatment of this injury in nearly all of the cases reported has been open reduction and internal fixation. As mentioned earlier, this injury may include a dislocation or subluxation of the talus in addition to the fracture. In such cases the talus usually cannot be completely reduced until the fibular fracture is reduced because of the traction-like attachments of the soft tissues from the displaced fibula to the talus and calcaneus. However, like most extremity fractures, an attempt at closed reduction should be made. This is done by placing the fingers on the fibular shaft and applying pressure posteriorly and laterally while inverting the ankle. If unsuccessful, an open reduction should be done. The fibular fracture is usually oblique and is in an anteroposterior plane. A posterolateral incision over the fracture site with a bicortical screw for fixation is recommended (Fig. 2-a). Following the reduction of the fibula fracture, attention should be directed toward proper treatment of the remaining components of this injury. This may require open or closed reduction, depending on the involvement of the talus and fractured tibia (Fig. 2-b).

Elmer R. Salovich, M.D.
Minneapolis, Minnesota

References

1. Bosworth, D. M.: Fracture-Dislocation of the Ankle with Fixed Displacement of the Fibula behind the Tibia. J Bone Joint Surg 29:130, 1947.

Derivatively Speaking

felon: from Latin *fel* meaning gall; hence something bitter or by extension, cruel or wicked.

Originality

If I could give an account for all that I owe to great predecessors and contemporaries, there would be but a small balance in my favor. — Goethe

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Forget the past. No man ever backed into prosperity. — Franklin Field

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Tumor Conference

Carcinoma of the Lung — A Rare Disguise

Carcinoma of the lung usually presents as a mass visible on chest x-ray. Frequently associated atelectasis or pneumonitis may be the predominant presenting sign. Occasionally we may see irregular cavitation within a large carcinoma as it outgrows its blood supply. It is rare that a small carcinoma will cavitate to present as a thin-walled peripheral cavity. Such a case is here presented.

Case Report

This man was 59 years old when he consulted his physician for a routine physical examination and advice about his bilateral inguinal hernias. The hernias had been present for a number of years and apparently had caused little discomfort. However, approximately three months earlier, he had taken a job which required more physical exertion than he had been formerly accustomed to. Associated with this increased activity, he had noted aching in the lower abdomen. He was asymptomatic as regards his chest. There was no known exposure to anyone with chest disease. He had not traveled beyond Chicago and Milwaukee. He smoked one and one-half packs of cigarettes each day.

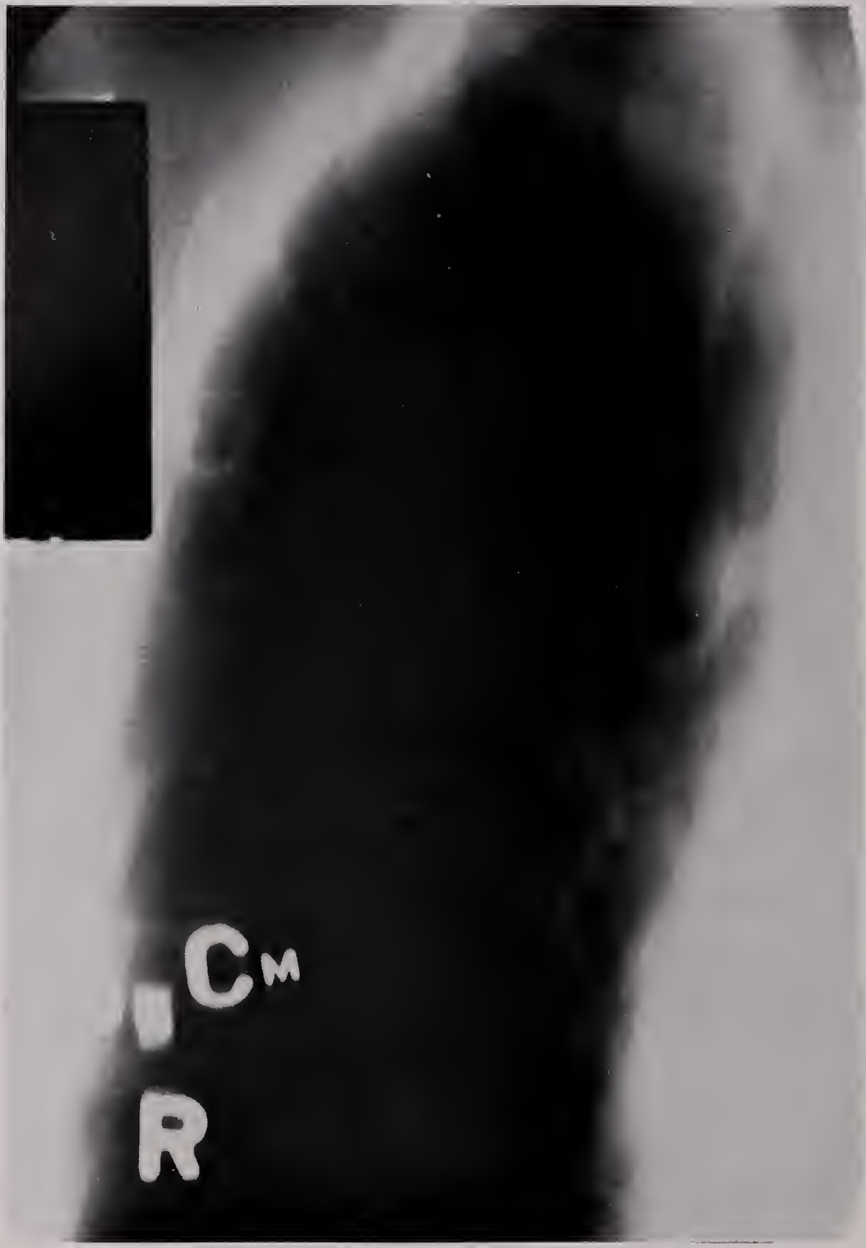
Physical Findings

Physical examination revealed a well developed, slightly obese 59-year-old male who was alert, cooperative, and did not appear ill. The blood pressure was 126/88. The remainder of his physical examination was entirely normal except for the following pertinent or positive findings. There were upper and lower dentures. There was no cervical adenopathy. The lungs were normal on physical examination except that the breath sounds were somewhat distant. Examination of the heart was normal. There were large bilateral inguinal hernias.

Laboratory Findings

Laboratory studies revealed the urinalysis to be normal. The hemoglobin was 15.2 gm. per cent. The white blood cell count was 7,590, of which 58% were neutrophils, 39% lymphocytes and 3% monocytes. The erythrocyte sedimentation rate was 57 mm. fall in one hour. The blood urea nitrogen was 12 mg.%. An electrocardiogram was normal. Seven sputa were negative for acid-fast bacilli and fungus on smear, and subsequently these were negative also on culture. Five gastric washing specimens were negative for acid-fast bacilli on smear and culture. Several sputa for tumor cells were negative. The skin test and complement fixation for coccidioidomycosis was negative. The tuberculin skin test showed over 2 cm. of induration. Chest x-ray on April 6, 1964, was normal except for a thin-walled ring like shadow in the right upper lobe at the level of the right second anterior space. This measured approximately 1.2 cm. in diameter. Planograms of this area revealed a thin-walled cavitary lesion best seen at the 10.5 cm. level.

Continued



Thin-walled cavitary lesion

It is our practice in the interest of avoiding postoperative complications to require that our patients be off smoking for at least two weeks before surgery. This patient was discharged to spend this period at home. Because of the possibility that the cavitary lesion was due to tuberculosis he received Isoniazid 300 mg. and P.A.S. 12 grams daily. He returned to the hospital and a right thoracotomy was performed. The cavitary lesion seen on x-ray was excised by scissors dissection and reported by the pathologist to show a very poorly differentiated carcinoma. A right upper lobe lobectomy and mediastinal node dissection was then performed. On his final report, the pathologist confirmed his frozen section diagnosis and suggested that the tumor most resembled a squamous cell type. Thirty-six nodes were examined and none showed evidence of metastasis. The postoperative course was uneventful. He subsequently has had repair of his inguinal hernias and to this date continues to be well and free of recurrence of his bronchogenic carcinoma.

Comments

Fanned by the high winds of modern sales techniques using every available medium to promote the use of cigarettes, an epidemic of lung cancer is raging across this land. Approximately 45,000 people, many at the peak of their most productive period, will die of carcinoma of the lung this year. Each year this number will increase to follow the rise in cigarette consumption. Until the general population is sufficiently enlightened to avoid cigarette smoking or until we understand the biology of cancer, our only defense is early diagnosis and adequate surgery. Early diagnosis will depend upon recognizing the enemy in each of its many disguises as readily as we do when it presents its usual appearance. The small thin-walled peripheral cavity which was this patient's bronchogenic carcinoma is a relatively rare disguise. The alertness and prompt action of his medical doctor fortunately lead to an early surgical attack with reasonable hope for cure.

This case is presented for the purpose of emphasizing the treachery of this disease and to publicize one of its less common disguises.

Frank E. Johnson, M.D.
Theodore A. Peterson, M.D.
Minneapolis, Minnesota

TRISOMY 13-15 (ALSO CALLED D TRISOMY) SYNDROME*

It has not been possible to establish whether the trisomy involves chromosome 13, 14, or 15; thus it is usually referred to as Group D Trisomy. This condition has been found in a number of newborn infants.

The cases are usually characterized by the following clinical symptoms: anophthalmia, cleft palate, harelip, polydactyly. The hands show horizontal palmar creases and relatively slim terminal phalanges with unusually convex fingernails. The thumbs can be bent backwards to an abnormal degree, sometimes referred to as "Trigger Thumb" (a better description might be "retroflexibility").

There may also be hemangiomata over the body and appendages, congenital heart defects, mental retardation, and early death.

Lee Schacht, M.D.
Minneapolis, Minnesota

TRISOMY 16-18 (ALSO CALLED GROUP E TRISOMY) SYNDROME*

It is fairly well established that this is a trisomy of chromosome 18. While this condition was thought originally to be very rare, with a full clinical description and chromosome analysis now available, it may be frequent as Trisomy 21 (Mongolism).

This disease is characterized by the following clinical description: ear deformities — low set, and sometimes malformed; spasticity due to a central nervous system defect; "Rocker Bottom" feet — an abnormal backward extension of the heel; flexion deformity of the fingers — the index finger over the middle finger when the fist is closed; micrognathia, umbilical hernia, congenital heart defects and failure to thrive — rarely surviving more than a few months.

Lee Schacht, M.D.
Minneapolis, Minnesota

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*See Minnesota Med 48:919, 1965.

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Neurological Conference

Hepatolenticular Degeneration*

Mentation —

Dr. Robert Soll: Hepatolenticular degeneration is a relatively rare hereditary disease appearing approximately once in 50,000 live births, an incidence similar to such heritable diseases as phenylketonuria. Our case today concerns a 26-year-old man with hepatolenticular degeneration.

Dr. L. R. Ringhofer:* In March 1964, I was called to the patient's home by distressed parents who told me that their son had lost consciousness. By the time I arrived, the patient had awakened, although he was somewhat groggy and had difficulty standing. I felt that he was having a post-seizure confusional state, and therefore I admitted him to the hospital for observation. As the patient's mental state gradually cleared, I was able to obtain a better history from him.

He is a young man who has been under the care of numerous doctors in recent years. His main concern was a shakiness of his hands, beginning at the approximate time of his divorce three years previously. In view of that history and a completely normal neurological examination except for a persistent mild tremor, I thought his trouble was probably more functional than organic. Only a year before another physician who had given him a complete workup in the hospital, had reached the same conclusion. At that time the patient had been placed on a tranquilizer which he had continued to take until the time of his unconscious episode.

Dr. Soll: Other than loss of consciousness and subsequent confusion, was there any other evidence that this may have been a seizure?

Dr. Ringhofer: There were no focal neurological findings. I was looking, of course, for a focal abnormality, but I found nothing except confusion and some unsteadiness when standing. The possibility that these might be functional or deliberate also occurred to me.

Dr. Soll: Did his parents witness the spell?

Dr. Ringhofer: Yes, it happened while he was taking a drink of water. Apparently he toppled over backwards in front of everybody. When he

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*Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatric conferences are held the first and third Wednesdays of every month from 3:15 to 4:15 p.m. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Charles Branthaver, in Pediatrics, and Dr. Robert Soll, in Adult Neurology. Conference held December 3, 1964.

*New Ulm, Minnesota physician.

Continued

didn't respond, they called me. The entire episode lasted about 15 or 20 minutes. By the time I arrived, he was sitting on the floor.

Mrs. Lora Lee Ruthenbeck:* We have known the patient ever since his admission to the St. Peter Hospital where he spent several months prior to his divorce in 1961. His marriage had been shaky from its beginning in 1958. He did not do well after his discharge.

Dr. Ringhofer: According to our clinic records, in 1959 the patient was noted to be withdrawing, negative and tense; psychiatric help was suggested then, but it was refused. Interestingly, on the occasion of his premarital examination in 1957, something about his general attitude must have been unusual, since the doctor whom he was seeing then advised him against marriage. This particular aspect of the history also fit with the idea of a functional type of problem. An intensification of these symptoms apparently lead to his admission to the State Hospital.

Dr. Joe Rich:** I first saw the patient on June 24, 1964, in New Medicine Clinic; he related essentially the same history to me as has been presented. Initially, I also felt that his problems were psychologically based. Apparently his hand tremors had increased markedly after his divorce, but then remained unchanged for six months before his visits here. On physical examination he had a wild flapping tremor of both arms and legs, worsened by any attempt to make an intentional movement. Also the tremor persisted when the patient was left alone by himself in the examining room: a fact which put my first impression on a somewhat shaky basis. The patient seemed to lose his balance very easily when standing or walking. Otherwise our initial neurological examination was not very decisive, since there were no other abnormal manifestations noted. Subsequently in Neurology Clinic, the Kayser-Fleischer rings in the cornea were noted and the tentative diagnosis of Wilson's disease was established.

The patient was admitted to the hospital on June 28, 1964. His serum ceruloplasmin† level was very low, varying from 9 to 12 units. The normal value for comparison has a range of 100 to 300 units.

Other liver function studies included a thymol turbidity — 3 units, a cephalin flocculation — 4 plus, and a BSP — 16% retention. The serum copper was less than 10 micrograms % and the urine copper was 0.056 mg./liter.

The patient was started on penicillamine, an oral chelating agent, in an attempt to increase his urinary excretion of copper. The initial dosage was 250 mg. four times daily, but it was eventually increased to 5 grams daily since an adequate increase in urinary copper was not obtained at lower dosages. In addition to penicillamine, a low copper diet, potassium sulfide and pyridoxine were also instituted. His first hospitalization extended from June 28th to August 11th, 1964. He was to return for a follow-up visit the last week in August, but he developed recurrent generalized seizures, which seemed to be more localized in his right upper extremity, and he therefore was readmitted to the hospital on September 5, 1964. After dilantin medication was instituted he had no further seizures. His tremors are diminished and there appears to be a decrease of the Kayser-Fleischer ring in the cornea.

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*County welfare department, Brown County.

**Student doctor, University of Minnesota Medical Center.

†An A^2 blue globulin having to do with copper metabolism.

Dr. John Brantner:[*] When I saw the patient he could not be tested for brain damage, nor could he take the multiphasic by himself. The method of having someone read it to a patient is of dubious value. The Peabody Picture Vocabulary test, requiring selecting from a number of pictures the one which is most appropriate to given words, suggested a firm IQ of 108, and the Binet vocabulary test, which requires word definition, indicated an IQ of 109; therefore, I think that we can say at the present time that his intelligence is approximately 110, the upper end of the average range of intelligence. As far as his personality is concerned there are, in the Binet vocabulary test, a few hints of some personality deviation: a slightly schizoid or near schizophrenic habit of thought. He seemed to be mildly depressed, but this is certainly understandable on the basis of his disorder.

His discharge diagnosis from St. Peter where he had electroshock therapy was schizophrenic reaction, acute undifferentiated type, but the reports do not give the results of their psychological tests. He told me that he had looked at his IQ when the examiners were out of the room, and his own idea is that his IQ is 167. He feels that he is an intelligent person and that his present IQ may represent some decline. I have no means of knowing, since there are no indications of central nervous system involvement in my testing. At the present time I can only report that he is of average intelligence, but with some tendency towards schizoid mentation.[**]

Miss Helen Kretchmer:[†] I saw the patient and his mother this morning. The mother has accompanied her son on other clinic appointments, since she felt a little reluctant to have him travel alone. Apparently there is a feeling of family solidarity. The father is a retired plasterer, 73 years old, on Social Security; the mother is somewhat younger and a housewife. There are only two children, the patient and his sister, age 36, who works as a bookkeeper. The patient related that he had been a polio patient at the Sister Kenny Institute when he was a child. The family lives in a home with two bedrooms upstairs and three rooms downstairs. When he first returned home from the hospital he had to sleep downstairs because he couldn't make the stairs, as there are some architectural barriers. A wheelchair was required when he was in the hospital, but now there seem to be no particular problems at home, since he is walking by himself. The family income consists of the father's social security, the patient's social security and the sister's earnings. The patient receives $103.00 social security, out of which he pays his family $50.00 for board and room, and about $6.00 for maintaining an insurance policy; he also spends $25.00 of his income for medication. I believe the welfare board authorized the rest of the hospital care here and helps to pay the remainder of the medical bill at home, assisting them with transportation when necessary.

I assume he is eligible for aid to the disabled, which could help cover medical expenses. There is a problem about which both the family and welfare board are concerned. Each penicillamine refill costs $22.50 and lasts only five days; the cost for this alone during the month is $135.00. There are some other expenses, but they are less significant. If he is going to be cared for regularly at this hospital, he may be able to get much of his

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[*] Clinical psychologist, University of Minnesota Medical Center.

[**] See Test Your Word Score Page 1029.

[†] Supervisor and assistant professor of social service, University of Minnesota Medical Center.

Continued

medication here, thereby using the county authorization to split the cost between the county and the state.

The patient said that he had 10 month's trial working experience at the rehabilitation center in Mankato following his 13-month hospitalization at St. Peter, mostly shoveling snow, mowing, and doing janitorial type work. This would indicate to me that they felt from their tests and from their experience with him that his potential was not too high. Apparently he was not placed in a job after that time. He has had an occasional day at work since then, one day as a truck driver and once with a garbage collector; that is about all.

When you mention his former wife or child, both he and his mother become distressed. His marriage was an extremely unhappy experience, and the family seems to think that it may have caused his illness.

As far as the present illness is concerned, the patient feels that he is better. He can dress himself except for buttons; also he can light a cigarette and hold it while he is smoking, which he couldn't do before. He is raising two rabbits now and hopes to raise more. Activities using large muscles are performed best, although he tires easily and his foot is unstable. Regarding amusement, I called the physical therapist and she suggested his using playing card holders which he can get through a commercial company. This would enable the patient to participate with the family when they play cards. He hasn't been very hopeful; but I think he and the family would welcome some type of occupational suggestion, either vocational rehabilitation or some type of home activity. Promoting this rabbit business or some other kind of work would give him some spending money.

Dr. Soll: Mrs. Ruthenbeck, how does your concept of the patient compare with this?

Mrs. Ruthenbeck: The family have always been very co-operative and appreciative people. I have just one question: if he continues to progress physically, should there be a change in the home situation; that is, should he be encouraged to go someplace else? I tried to talk to him about this, but I wasn't very influential with him. There is a great dependency upon the mother, who is very dominating with both the husband and the son. The patient is too dependent upon her; however, during the present illness he needed someone else to help him.

Dr. Soll:

Two fairly distinct categories of patients having hepatolenticular degeneration have been described.[1]

Pseudosclerosis

One type was described by Westphal in 1883 and was termed "pseudosclerosis." Its onset usually occurs between 19 and 35 years of age and is characterized by a slowly progressive course. Chief difficulties are dysarthria and tremor with very little dystonic fixity of posture. A patient may also have cirrhotic liver disease as evidenced by a positive thymol turbidity or cephalin flocculation, but usually there are no symptoms referable to hepatic involvement until late in the disease when ascites may appear.

Progressive Lenticular Degeneration

In 1913, Wilson described the second form of this disease which he called "progressive lenticular degeneration." This type has a much earlier onset, usually between seven and 15 years of age, and is characterized by dystonia with very abnormal postures as the first sign. There may be rapid finger tremors; but the often described "wing flapping" occurs late if at all. At times myoclonic jerking may be seen. Hepatic symptoms likewise may be noted in the patient or in his family. The terminal picture in this type of the disease is one in which the limbs are rigidly semiflexed. The course, as a rule, is quite irregular with sudden severe relapses; response to therapy is poor, and survival is often less than four years. This picture contrasts considerably with those patients having the pseudosclerotic type of Wilson's disease, not only in the clinical picture, but their response to treatment is also much better in pseudosclerosis. Survival tends to be longer in pseudosclerosis and many patients have been reported to live 10 to 15 years after onset of symptoms.

I believe our patient falls into the category of pseudosclerosis, and therefore his prognosis would be much better than in the progressive lenticular degeneration type. Even in pseudosclerosis the prognosis is not the best, but he may continue to live a fairly comfortable life for several years. In view of this, I believe the patient could continue to live with his parents until such time as he is no longer physically or mentally competent.

Dr. Milton Alter:* The disorder is now established as a recessive trait, which means that the affected individual is a product of parents both of whom are carriers of the trait. The fact that our patient is affected is evidence that both parents must be carriers.

Ceruloplasmin

Exactly what is inherited here is not known, but a feature which has been found in almost all case studies is a low to absent level of a certain protein in the body called ceruloplasmin, which means literally 'blue protein.' This is a protein manufactured by the liver, the function of which is to bind copper absorbed from the intestinal tract. All of us need a certain amount of copper in our metabolism, and the regulation of the level of copper in the body is largely a function of this particular protein. It is a situation analogous to iron; iron is needed for a number of functions in the body. The situation with copper metabolism is similar in that we absorb a certain amount of copper from the diet. Initially this copper is bound to albumin. This is a very transient binding, and the copper is then released to enter various metabolic pathways. Some of it is bound by ceruloplasmin, which is a much stronger and more permanent binding for most of the copper in our body. If we have inherited the inability to make ceruloplasmin or if we have inherited defective ceruloplasmin which doesn't function properly, then our copper metabolism is abnormal. In this abnormal state, copper is first bound to albumin, but is then released and deposited in tissues where it should not be.

Lenticular Degeneration

The basal ganglia of the brain where the lenticular nucleus is located is one of the tissues where copper is deposited in this disturbed copper metabolism; hence the name "lenticular degeneration." This is thought to be the basis of the abnormal movements observed clinically. Copper is also

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*Instructor, department of neurology, University of Minnesota Medical Center.

Continued

deposited in excessive amounts in the liver, probably causing the cirrhosis which is so common in this disorder. There is also an excess amount of copper in the kidney, which poisons enzymes necessary for renal tubular reabsorption of various substances; hence, people with Wilson's disease will spill amino acids into the urine because they can't retain them. Glucose metabolism is impaired. There is an excess excretion of uric acid and copper, and phosphorus metabolism is also handled in an abnormal way, presumably because of the poisoning of the renal enzymes. This gives rise to a whole host of problems other than the brain and liver problem which we have already mentioned.

Kayser-Fleischer Ring

Copper is also deposited in the cornea of the eye, forming a ring of pigmentation which was described by Kayser and Fleischer; the ring is named after them, the Kayser-Fleischer ring, and it is not found in any other condition. It is not present in all patients; but if it is present, it is considered pathognomonic of the condition. An analysis shows that the pigmentation in this ring is, in fact, copper. So the basic defect is a deficiency of the copper-binding protein, ceruloplasmin; consequently, the individual with Wilson's disease cannot handle copper properly.

Carriers

This patient has had a son, and the question arises: could he be affected? The answer is probably no, because the condition is so rare that it is unlikely that the patient married another carrier. The child might be a carrier but will not be affected by the disease. In carriers that have been studied, lower than normal amounts of ceruloplasmin have been found. Unfortunately some people who are not carriers also have rather low amounts of this protein. Thus, there is not a clear-cut demarcation, but on the average, carriers will show a lower amount of ceruloplasmin than the normal individual. This is probably due to the fact that one of the chromosomes in carriers can direct the production of ceruloplasmin, while the homologous chromosome cannot.

Actually, there are three genetic possibilities in this family. One fourth of the children of carriers may be entirely normal; one half may be carriers and not manifest the disease except on chemical analysis of the ceruloplasmin level, and one fourth may be affected. The likelihood in the sister's case is that she is not merely a carrier but is affected with the disorder.

In a study of fingerprints of those having this condition there is a characteristic deviation from normal in the fingerprint pattern in that patients have a excess number of whorls. Basically, there are three types of patterns: loops, arches and whorls. The normal frequency of whorls is about 30% and a high proportion of the people with Wilson's disease have an excess of whorls. This happens to be true in the patient and in the sister. Nine out of ten of the patterns were whorls in the sister; she had even more whorls than the patient.

Provocative Test

The clinical diagnosis may be aided by finding an excessive amount of copper in the urine. Sometimes this isn't found even in a known case. However, if penicillamine is given to these individuals, a release of the copper occurs which may then be detected in the urine. Penicillamine administration can be of diagnostic help as a provocative test. In a normal individual penicillamine will not cause excessive amounts of copper to be excreted.

Dr. Soll:

There are at least two schools of thought on this disease as far as treatment is concerned. On the one hand, Scheinberg[2] from the Albert Einstein Hospital in New York is quite enthusiastic about treating the patient with chelating agents such as penicillamine. He feels that this is extremely important and should be used in all patients, even to the extent of screening young children for the disease in much the same manner as is being done for phenylketonuria. He would maintain that if the disease is found early in life, much of the neurological deficit due to copper deposition in the tissues would be prevented or at least delayed. On the other hand, Denny-Brown from Boston was quite pessimistic about the prognosis of the disease even with treatment. He felt that not all patients responded favorably, particularly that group which has progressive lenticular degeneration. Patients with predominantly tremor responded best, whereas those with dystonia were benefited very little if at all. Brown also cited several instances in which episodes of hepatitis produced a clinical picture not unlike the dystonic type of Wilson's disease, but without any abnormality in copper metabolism. Because of these facts he felt that there was also some other factor involved besides abnormality in copper metabolism itself.

Dr. Alter: I am familiar with both schools of thought and with the opinion that therapy may not really alter the course of the disease very much. I personally have seen about six cases of this condition. I recall most vividly a young girl who was treated with penicillamine; she declined exceedingly fast and died of liver failure about a year after the diagnosis was made. I myself am rather pessimistic about the long term outlook for these people. However, research may well uncover a means of helping patients with Wilson's disease and we should certainly be hopeful.

Dr. Rich: The patient's sister has been tested and she has also been found to have evidence of the disease. Her laboratory data include the following: cephalin flocculation — 4 plus; serum ceruloplasmin — 13 units; and serum copper — 22 micrograms %. Although these tests are abnormal, she has very few neurological manifestations. Tremor has been noted, but it is not present at all times; some mental changes have been evident.

Dr. Soll: A very important question is: how effective is the treatment? If it really delays onset of the clinical symptoms as well as reducing symptoms already present, siblings of those who have the disease should be evaluated for treatment. Dr. Blain has been considering this problem and I'd like to ask his opinion on what he thinks should be done with the patient's sister.

Dr. Gilles Blain:* First of all, I would like to be optimistic. Many patients who have been treated with chelating agents such as BAL (British Anti-Lewisite) or penicillamine were definitely improved, and statistically, their

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*Medical fellow specialist, neurology, University of Minnesota Medical Center.

Continued

longevity was increased, when compared to untreated individuals. So I don't think that we can say that penicillamine only improves the symptoms without increasing the longevity. It appears that it really may do both. As far as the family is concerned, the sister is involved with the disease and before we start her therapy we want to hospitalize her to obtain some base-line studies. We would also like to study the parents if possible in order to find out more about the carrier state.

Further Studies

We propose to do a liver scan, using a radioactive copper with a short half-life of about 12 hours. We would also like to further study the psychometrics, particularly in the patient and in his sister, as well as give them the battery of tests we use for our patients with vascular disease. We have done a tryptophan loading on the patient already, before he received penicillamine, during penicillamine therapy and during penicillamine and pyridoxine therapy. The reason for this is that tryptophan is involved along with B6 metabolism and one form, L- penicillamine, apparently does depress the metabolism of B6. This came up very abnormal, both during the controls as well as during the loading with tryptophan and B6. We want to repeat this on the whole family to determine if there is any abnormality. This could be due to a block in the metabolic pathway of tryptophan, or it could also be due to damage from the copper as was mentioned by Dr. Alter.

Dr. Soll: I'd like to mention the toxicities that may occur. These should be checked for frequently when penicillamine is first instituted. Rash, fever, and lymphadenopathy are perhaps the most common complications. An iron deficiency anemia may develop since penicillamine will combine with metals other than copper, but this can be corrected by simply supplying additional iron to the diet. More rare complications include skin dryness, nausea, purpuric and sometimes vesicular hemorrhagic lesions. Cataracts have been noted to appear during the course of therapy in a few patients. Renal nephrosis has also been seen which tends to improve if penicillamine is discontinued. Because of these various complications, early during the course of penicillamine therapy frequent blood counts and urinalysis should be obtained, and the patient himself should be closely observed.

The entire outline of treatment should include a low copper diet, aiming at a total copper intake of less than one milligram per day. Penicillamine may be started at 1.0 gm. daily in divided doses, and then gradually increased until the urinary copper excretion exceeds 1.0 mg./day. Doses of penicillamine greater than 4.0-5.0 gm. daily usually to not increase further copper excretion. To supplement the low copper diet, potassium sulfide is administered with meals in order to bind copper present in the food before it is absorbed into the body. In this way we attempt to maintain a negative copper balance. Pyridoxine may be supplemented in the diet because of the possibility of interference in its function by penicillamine.

Conclusions

1. The patient should continue living at home and, with the help of social welfare and vocational rehabilitation, he should be encouraged to pursue a simple occupational project.

2. Treatment of the patient's sister should be instituted in an attempt to prolong the appearance of neurological complications in her.
3. An attempt should be made to obtain as many of the previous psychological tests as possible, and further psychological testing should be made periodically in the future in order to evaluate fully any significant deterioration in the patient's mentation. This will also help to assess the effects of the penicillamine therapy on the course of the disease.
4. Regular urinary copper determinations should be done in order to maintain the penicillamine at optimal dosage; this will help keep cost of medication at a minimum level.

Robert Soll, M.D.
University of Minnesota Medical Center

Participating in the conference: Joe Rich, student doctor; Dr. John Brantner, clinical psychologist (University of Minnesota Medical Center); Miss Helen Kretchmer, supervisor and assistant professor of social service (University of Minnesota Medical Center); Dr. Milton Alter, instructor, department of neurology (University of Minnesota Medical Center); Dr. Gilles Blain, medical fellow specialist, neurology (University of Minnesota Medical Center); Dr. L. R. Ringhofer, New Ulm, Minnesota; Mrs. Lora Lee Ruthenbeck, county welfare department, Brown County and Dr. Robert Soll, chairman, adult community services (University of Minnesota Medical Center).

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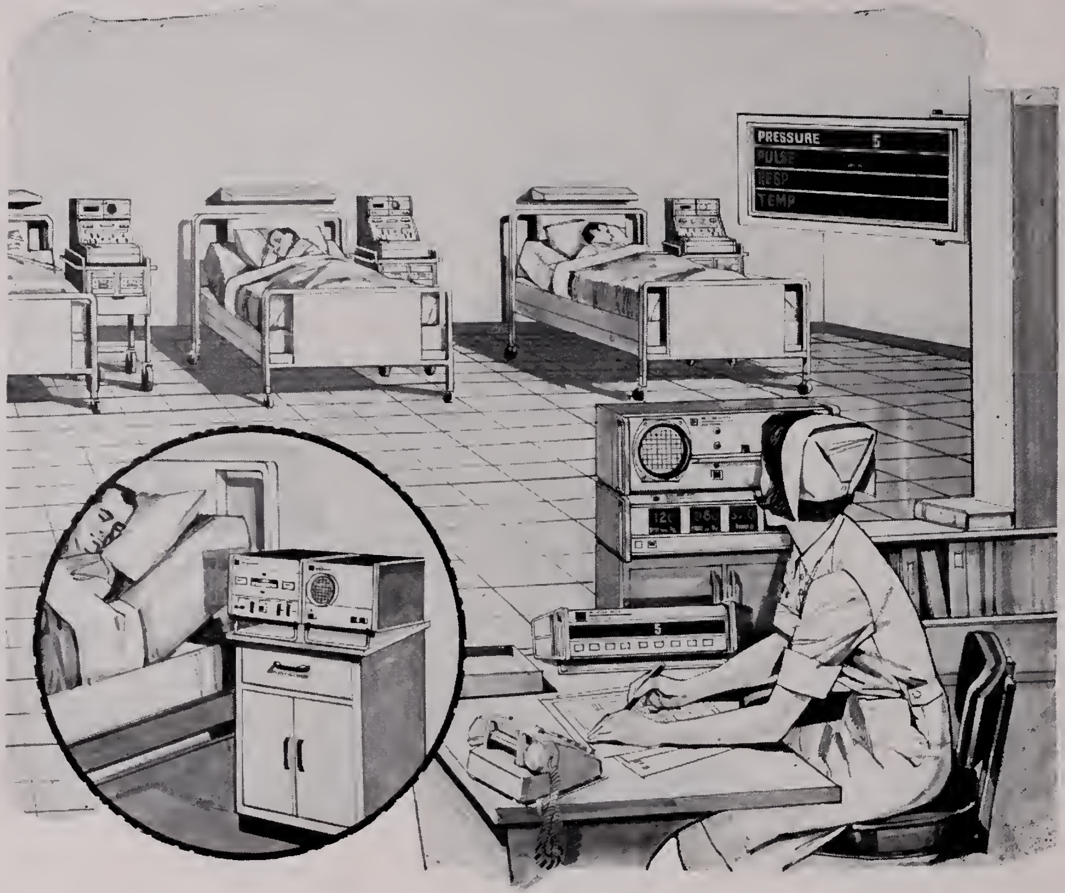
Silphium

Rating high in ancient pharmacopoeias was the herb drug silphium. Just what silphium was is undetermined, as pharmacologists have been unable to identify it with any of our modern plants or herbs; but its phenomenal use in ancient times is a matter of record. Its efficacy against malaria, toothache, rabies, tuberculosis, pleurisy, jaundice, sore throat, whooping cough, and miscellaneous wounds was attested to by Dioscorides, Pliny, Hippocrates, Galen and Celsus. Notwithstanding the endorsement of such notables, the modern world remains justifiably sceptical of such therapeutic versatility for any drug.

However, the demand for silphium was so great that fortunes were amassed by enterprising individuals with sufficient foresight and acumen to monopolize the supply and manipulate the market. Julius Caesar is reputed to have become such a silphium capitalist. Also one Hamuel, doctor and priest in ancient Egypt, is said to have profited handsomely by trafficking in silphium imported from Lybia — unbeknown to the custom officials.

Speculation on the identity of silphium suggests that it may have been a plant similar to laserwort or frankincense — used for fumigation and in embalming; or it may have been the prosaic asafetida, an herb with a garlic-like odor and taste, sometimes employed medicinally as an antispasmodic, especially by some sects, one of which in their excessive prudery preferred to call it rumpafetida.

But whatever silphium was, it could not have been the wonder drug it was purported to be. Had it been such, its loss to posterity would have been an irreparable one.



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Grand Rounds

Surgical Treatment of Obesity*

There are many reports of survival after massive small bowel resections performed because of infarction and neoplasm.[1,3,8,11,13] A number of studies have been made of the amount and level of small bowel resected and the resulting nutritional status of patients and experimental animals. These studies have produced a better understanding of the small intestine and the permissible limits of resection, and stimulated the consideration of surgical bypass of the small bowel as a means of treating extreme obesity.

Weight Loss Following Small Bowel Resection

Kremen et al.[1] studied dogs divided into five groups, three animals in each group, and reported the following results:

In Group I, animals who had the proximal 50% of small bowel removed from intestinal continuity had lost 15% of their preoperative weight at seven weeks, but by 24 weeks had regained their normal weight. After 24 weeks these same animals had, in addition to their previous resection, an ileocecal valve bypass performed without significant change in their normal weight.

Group II consisted of animals who had the distal 50% of small bowel bypassed, from 3 cm. proximal to the ileocecal valve extending cephalad. These animals exhibited progressive weight loss equal to 15% of their body weight by 15 weeks postoperatively and stabilized at this weight for the following nine weeks. At 24 weeks the distal 50% of bowel was returned to intestinal continuity and the proximal 50% removed. They gradually regained weight and in 14 weeks were back to their original weight.

Group III animals were similar to Group II except that the ileocecal valve was bypassed. This group lost weight steadily and exhibited the most profound cachexia of all the groups, showing no tendency towards

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*Presented as a Medical Grand Rounds at Mt. Sinai Hospital, Minneapolis, January 12, 1965.

Continued

compensation or stability. These animals then had the ileocecal valve replaced into continuity. Only one animal survived this second procedure, but consequently stopped losing weight.

Group IV had the proximal 70% of small bowel removed. This group lost about 5 % of their preoperative weight and stabilized at this level.

Group V had the distal 70% of small bowel removed and consequently lost about 20% of their preoperative weight and stabilized at this level without any apparent ill effects.

Levin et al.[4] studied a 42-year-old, 192-lb. white woman who had 237 cm. of small intestine from distal duodenum to within eight inches of ileocecal valve removed for a tumor. The remaining duodenum was anastomosed to the terminal ileum. Three months after the operation she was having two to four yellow, steatorrheic stools per day. Two years later her weight was about 93 lbs. and remained at about this level for the succeeding four years.

Weckesser et al.[10] in a study on animals with two thirds of their proximal small bowel removed found a 14% weight loss at five weeks postoperatively with stabilization at about 15 weeks with 24% weight lost.

Fat, Nitrogen and Water Balance Studies Following Resection

In Kremen's study[1] those animals in which the distal small bowel was diverted from the intestinal stream had a consistently high loss of fat in the stools. In groups where the proximal small bowel was out of intestinal continuity and the distal small bowel in place, the fecal fat losses were only slightly above control values. Bypass of the ileocecal valve did not appear to alter the efficiency of fat absorption in groups with the proximal small bowel removed. Similarly, in groups with the distal bowel resected and also ileocecal valve bypass no significant added effect on fat absorption was noted. No important increases in fecal nitrogen loss over control levels were observed where the proximal small bowel was removed, whereas moderate but significant increases in fecal nitrogen excretion occurred with diversion of the distal small bowel.

Fecal balance studies on 25 patients with small bowel resection were carried out by Kalser et al.[3] These resections were performed for a variety of reasons: adhesions and obstructions, gangrene and chronic inflammatory intestinal disease.

The patients were classified into groups on the basis of the extent of small bowel resected or bypassed and type of anastomosis used: Group I: six patients with less than two feet of small bowel resected; Group II: 14 cases with three or more feet of distal small bowel and adjacent colon resected so that the terminal ileum and ileocecal valve were removed; Group III: five cases with seven to nine feet of small bowel removed, but a segment of terminal ileum varying from 10 inches to two feet and the ileoceal valve and the colon undisturbed (Table 1).

These investigators[3] concluded that resection of two feet or less of ileum did not result in significant steatorrhea, but extensive resection of small bowel did result in marked steatorrhea. In those patients with a segment of terminal ileum and the ileocecal valve intact, the fecal fat was only one third as high.

Kreman et al. concluded that 50-70% of proximal small intestine of dogs can be removed with no apparent ill effects. Weight is maintained and protein and fat absorption are not significantly altered. Sacrifice of the distal

50% of small intestine produces a profound interference with fat absorption associated with weight loss. The ileocecal valve appears to have an important effect on the nutritional adjustment to sacrifice of the distal small bowel, but appears less important in sacrifice of the proximal small bowel.

TABLE I
Fecal Balance Studies[3]

Group	Wet Weight of Stools Average	Range	Fat Average	Range	Nitrogen Average	Range
	gm/day		gm/day		gm/day	
I	760	250-1800	5.7	2.4-14.2*	3.0	1.0-5.8
II	1500	420-6500	42.8	8-97	6.8	2.6-10
III	240	120-300	11.6	8.0-15.0	2.2	1.3-3.0

*Normal fat excretion in four of six cases of Group I. All in Group II and II were abnormal.

Serum Cholesterol, Lipoprotein, Plasma-Free Fatty Acids and Carotene Concentration after Small Bowel Resection

Two obese female patients were studied to determine the effect of decreasing the absorptive area of the small intestine on concentrations of serum cholesterol, lipoproteins, plasma free fatty acids and carotene.[7] Two to three years after removal of all but about 15-20 inches of jejunum with jejuno-colic anastomosis, their body weights were stable at about 90 lbs. less than preoperative levels. Serum cholesterol and beta-lipoprotein concentrations were sharply decreased to less than 50% of preoperative levels. A normal increase in concentration of plasma-free fatty acids occurred with fasting. The serum protein pattern was not changed as a result of operation.

Anemia after Small Bowel Resection

A severe megaloblastic anemia* with hemoglobin concentrations ranging from 3.8 to 7.3 gm. occurred in five of 14 cases with extensive resections of the small bowel and ileocecal valve.[3] The onset of anemia was 18 to 66 months after surgery. It was concluded that the ileum was more concerned with vitamin B_{12} absorption than the jejunum.

In Weckesser's study[10] seven of 12 animals developed anemia several months after a two-thirds resection of small bowel. In all cases this was a hypochromic anemia. Macrocytosis was not observed.

Compensatory Mechanisms

Butler[6] has pointed out that after small bowel resection, the remaining bowel increases in size and thickness to expand the absorptive surface and the patient loses weight, so that there are reduced caloric and protein requirements, and finally intestinillization of the colon occurs to compensate for the loss of absorptive surface. He claims there is a large factor of safety in the amount of available absorptive surface of the small intestine and only one half of the available absorptive surface is required. If less than one half of small bowel is lost, no compensatory mechanisms are required. If the loss is greater, compensatory changes can be anticipated.

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*See Test Your Word Score Page 1029.

Continued

Amount of Small Bowel Safely Removable

From the experience of Weckesser et al.[13] and others, it can be concluded that the response to resection of small bowel is quite variable. Many factors, such as health, age of the patient and health of the remaining segment of the intestine, are important. It appears that distal resections of the small bowel are less well tolerated than proximal resections. In general resections of 20-50% are well tolerated and many patients do well after greater percentages removed.

Sullens[16] states that 50% of small bowel can be sacrificed without persistent untoward effects, but that after removal of 75%, inanition and eventual death usually result. Resections of proximal bowel are generally better tolerated than resections of the distal bowel.

Clinical Summary

A 30-year-old white female had been followed for problems of uncontrolled obesity since age eight. A variety of diets had been tried but had failed to control her weight. She was admitted to the Mount Sinai Hospital Medical Service on 11-16-64, at which time her weight was 386 lbs. and her height 5′5″.

Past history revealed known moderate hypertension since a toxemia pregnancy 10 years before. She had had a tonsillectomy but no other surgery.

Laboratory studies revealed a normal blood urea nitrogen, creatinine 0.9 mg%, uric acid 6.2 mg%, total serum protein 7.5 mg% with 4.2 mg% albumin and 3.3 mg% globulin. Cholesterol 243 mg%. Normal hemogram and urinalysis. CO_2 29 mEq./L., chlorides 102 mEq./L., sodium 136 mEq./L., potassium 4.2 mEq./L., calcium 8.7 mg%. Bromsulphalein liver function test showed 4% dye retention at 45 minutes. Fasting blood sugar was 130 mg%. Alkaline phosphatase was 4 K.A. units. Serum carotene was 157 mcg% (normal 50-300 mcg%). Thyroid function studies were normal.

A cholecystogram was normal, as were a chest x-ray and an electrocardiogram. Studies of adrenal cortical function, including urinary excretion of 17-hydroxycorticoids and 17-ketosteroids, and response to ACTH were normal.

On November 27, 1964, surgery on the small intestine was performed as treatment for the extreme obesity. The length of the entire small bowel was 14 feet. The jejunum was transected proximally 10 inches distal to the ligament of Treitz. The ileum was then transected 25 inches proximal to the ileocecal valve. The proximal ileum was anastomized to the transverse colon to drain the bowel taken out of continuity. Upon completion of this part of the operation an anastomosis was then performed between the proximal 10 inches of jejunum and the distal 25 inches of terminal ileum. The patient thus had 35 inches of small bowel in continuity and approximately 11 feet of small bowel out of intestinal continuity. She had an uneventful postoperative course. By December 7, 1964, her weight had decreased from 386 lbs. to 347 lbs. She was placed on a regular diet and discharged from the hospital on December 7, 1964.

The patient was readmitted to the hospital on 12-24-64 because of a wound infection. Her weight at this time was 334½ lbs. and she had been feeling well. For the first 10 days post operation she had about 12 very loose watery bowel movements each day, which now had decreased to three formed stools in the morning and three loose stools in the evening.

Julian Ferstenfeld
Medical Student Extern
Mt. Sinai Hospital

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10-16 May be secured from Grand Rounds Editor.

TURNER'S SYNDROME*

In this syndrome, there are several congenital anomalies consisting of iliac horns, dystrophy of the nails, anomaly of the patellae, chondrodysplasia and arthrodysplasia of the elbows. This condition is transmitted as a dominant hereditary character.

Most of the anomalies are essentially asymptomatic. The iliac horns are usually found in routine roentgenograms, but the finding of these suggests the presence of other abnormalities, namely the underdevelopment of the nails of the thumb and the index finger, with less constant anomalies such as a defect of the radial head, prominence of the acromion and clavicle, underdevelopment of the scapula and discoloration of the iris. In this syndrome there is a chromosome anomaly of the sex chromosome.

— Robert Durham, Encyclopedia of Medical Syndromes, Paul B. Hoeber, Inc.

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*See Minnesota Med 48:919, 1965.

Anatomists see no beautiful women in all their lives, but only a ghastly sack of bones with Latin names to them, and a network of nerves and muscles and tissues inflamed by disease. — Mark Twain

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Faith may be defined briefly as an illogical belief in the occurrence of the improbable. — H. L. Mencken

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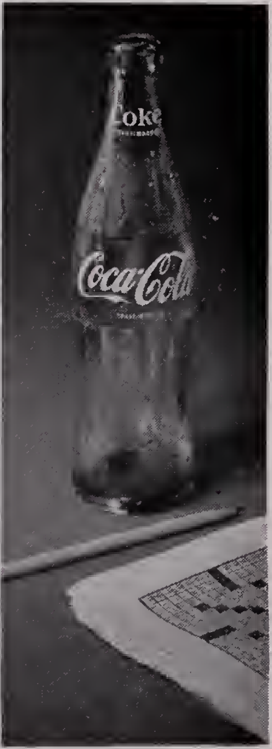

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Abstracts, Briefs and Commentaries

DUMPING AND MALNUTRITION

This author is concerned with dumping, and has made certain studies and observations which appear to offer significant contributions to this almost overworked problem. He points out that the severe dumper is, in fact, relatively rare; but when the problem does exist to a severe degree, it is very serious. He applied his procedure to only eight patients over a period of eight years. They had not responded to any other procedure and had had weight loss on an average of about one third of their body weight before undergoing his procedure.

In order to eliminate the emotional and psychogenic factors and ascertain a true physiologic origin of the problem of the patient suspected of dumping, the investigators have induced the symptoms with 50% glucose into the pouch, but have mainly placed reliance on the absence of dumping symptoms when the patient was given 500 cc. of 5% glucose in normal salt solution in the course of one-half hour preceding a regular meal and an additional 500 cc. during the meal.

The corrective procedure involved the construction of a short reverse or antiperistaltic segment of jejunum. Following this procedure cineradiographic studies revealed that pouch-emptying following the corrective operation occurred more by dilution of contents by saliva, succus entericus and refluxed fluids from the duodenum, and piecemeal passage through the reversed segment, rather than by the usual peristaltic action, thus sufficiently slowing the pouch-emptying to prevent the postgastrectomy dumping syndrome.

Several studies and attempts at changes in the outlet or substitution of a portion of the pouch by other bowel have been performed, but in general have essentially failed. The major difference is the reversal of polarity or use of an antiperistaltic segment of bowel in Dr. Poth's procedure.

J. H. Strickler, M. D.
Minneapolis, Minnesota

Poth, Edgar J.: Surgical Correction of Severe "Dumping" and Postgasterectomy Malnutrition. A Therapeutic and Diagnostic Test. Ann Surg 160:488, 1964.

TREATMENT OF DECUBITUS ULCERS

When absorbable gelatin sponge (Gelfoam) was used in addition to the usual treatment for decubitus ulcers in 24 patients, fine, healthy granulations appeared quickly, and the wounds healed in an average of 30 days. Such rapid healing has not been obtained with the usual treatment, which includes: treating the patients on turning frames, maintenance of good nutrition, between-meal feedings, and the administration of antibiotics to which the cultured organisms are sensitive.

All wounds were free of necrotic tissue when treatment was initiated; this was accomplished by debridement when necessary. Culture and sensitivity studies revealed that most wounds contained resistant Staphyococcus aureus, along with the usual fecal organisms. Secretions, which varied from excessive to moderate and were purulent, became clear and diminished sharply in volume within several days after initiation of treatment. Laboratory studies of the secretions have not, as yet, been helpful in establishing a possible reason for the effectiveness of treatment.

The absorbable gelatin sponge (20 mm. x 60 mm. x 7 mm.), which is compressed in its sterile wrapper, was removed with sterile forceps and inserted into the deepest or most undermined portion of the wound once a day. No other treatment, e.g., skin cleansing or irrigation with solutions, was used. Dressings were not needed in most cases, but they were used if the material might fall out.

The clinical trials were undertaken after dramatic results were obtained when absorbable gelatin sponge was placed in a large ulcer of a paraplegic dog; the wound was healed in 1 week.

Courtesy of Farley Manning Associates
New York, New York

Freeman, L., Joyner, J.: JAMA 184:784, 1963

GALACTORRHEA

Seventy-one cases of non-puerperal galactorrhea are reviewed. Galactorrhea was categorized as either primary or secondary. Patients with primary galactorrhea, or the Argonz-del Castillo syndrome, were those who produced a milk-like secretion which was not connected with pregnancy. The secondary group was comprised of those patients who had been pregnant and who exhibited the Chiari-Frommel syndrome, characterized by post-puerperal galactorrhea, amenorrhea, and ovarian uterine atrophy. Eight of the 17 patients in this group had evidence of tumor. Two of the women in the group without evidence of tumor became pregnant during the period of observation, the galactorrhea persisting during pregnancy. Evidence of a pituitary adenoma was found in three patients with the Argonz-del Castillo syndrome. Three women with acromegaly and one with a craniopharyngioma also had galactorrhea. In 42 patients various endocrine deviations, mainly menstrual disturbances, but also thyroid disease, obesity and hirsutism, were accompanying disorders. Imbalance in the function of endocrine glands is pointed out as a possible cause for the appearance of galactorrhea in most of the patients.

Courtesy of References and Reviews
Journal of the American Medical Association

Bercovici, B., and Ehrenfeld, E.: J Obstet Gynaec Brit Emp 70:295, 1963

COLLAGEN SPONGE FOR DIFFICULT OOZING

Peacock, Seigler and Biggers used tanned collagen sponge bovine tendon by the Eskon Laboratory in experiments on liver to control the surface oozing which would be evident after liver rupture. The collagen sponge graft could be a valuable technical adjuvant in the care of wounds of cellular organs or large surfaces where capillary hemorrhage is extensive and temporary fibrous tissue support is needed.

They found no antigenicity in the collagen sponge and no unfavorable reaction.

The fact that collagen sponge provides a temporary fibrous template for a new connective tissue synthesis and is completely absorbed in eight weeks indicates that it does have a value for the purpose for which it was intended.

The experimenters considered it to be contraindicated as a substitute for dura mater and to be of no value in reinforcing or adding tensile strength to wound deficits, such as large hernias. Likewise, it should not be used to restore or develop contour in cosmetic surgery.

It is suggested that in large areas of minor oozing, such as in places where gauze sponge is temporarily applied and removed at a later date, the tanned collagen sponge placed between the tissue and the gauze sponge serves to diminish the recurring oozing after the gauze sponge is removed.

There are instances in which continuous oozing is an annoying post-surgical complication. The tanned collagen sponge would seem to provide some value in these cases.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Peacock, Earl, E., M.D., Seigler, Hilliard F., M.D. & Biggers, Paul W., M.D.: Use of Tanned Sponges in the Treatment of Liver Injuries. Surgery 161:238, 1965

CONTUSION OF THE HEART

Demuth and Zinsser indicate that contusion of the heart occurs more often than is usually recognized. They add seven cases to the literature.

The history is relied upon for a definite injury usually to the chest or precordium and they suggest that though most authorities have stated that the large majority of patients recover uneventfully, their experience is that death may develop, unrecognized as having been caused by the injury. Of their seven patients, three died within the first twenty-four hours, three died between the first and the sixteenth day and one survived.

They indicate that the pathology is then similar to that which is observed from infarcts.

If the patient survives the first week after injury, complete recovery usually occurs, though late incapacity may result.

Treatment is similar to that which is given for coronary disease, except that if a definite diagnosis of contusion is made, it is probably inadvisable to use anticoagulants in a bruised heart because of the danger of extending the hemorrhagic process.

They note that with the increased incidence of car accidents, it would be well if cardiac evaluation be made immediately after the accident in order to allay unfair claims of heart damage at a later date.

J. H. Strickler, M. D.
Minneapolis, Minnesota

Demuth, William B., and Zinsser, Harry F.: Myocardial Contusion. Arch Int Med 115:434, 1965.

MEASLES VACCINATION

The inadvertent introduction of measles into a children's hospital ward occurs frequently and offers a special threat to the tuberculous child. The measles vaccine was used as a prophylaxis after measles contact within a closed population of children under therapy for tuberculosis. The expected outbreak of regular measles was aborted. Signs and symptoms observed were similar to those in normal children who have been given the vaccine. The vaccinated children were protected from reinfection when regular measles was reintroduced into the ward.

Courtesy of References and Reviews
Journal of the American Medical Association

Berkovich, S., and Starr, S.: New Engl J Med 269:75, 1963

THE FAMILIAR FACE

This paper presents an attempt, on the part of the hospital physician, to cope with the "Thick File Case." This clinical picture shows a high frequency in middle-aged women, with many years of regular attendance on the same family doctor, a full social and domestic life, multiple references and investigation without disclosure of significant organic disease, and failure in many cases to respond to symptomatic therapy or psychiatric treatment. The proposed management of such cases is that of detachment from the family doctor, attachment to a follow-up clinic at hospital, and guidance from one physician, also an attempt to uncover to the patients the emotional situations, and to explain the harm and damage being done to themselves and their family by this constant pursuit of ill health. Complete return to normal health is possible at any stage, providing the patient accepts and acts upon strong advice on re-orientation.

Courtesy of References and Reviews
Journal of the American Medical Association

Kemp, R.: J Lancet 1:1223, 1963

CARCINOMA OF CERVICAL STUMP

Of a series of 163 carcinomas of the cervical stump, 81 were classified as carcinomas of the true cervical stump, because the symptoms leading to the diagnosis developed 3 years or more after subtotal hysterectomy for a benign condition. Cases in which symptoms appeared before completion of the third postoperative year were designated as "coincidental." The cases of carcinoma of the true cervical stump in this series represented 4.5% of the total number of cervical carcinomas seen during the same period (1910-1960). The rapid increase in frequency of coincidental carcinoma of the cervical stump in the authors' material leads them to predict that carcinoma of the true cervical stump will also disappear within the next 20 years. In the coincidental series it was found possible to predict the occurrence of persistent cancer from the abnormal findings on the intravenous pyelogram. In the authors' experience, integral roentgen therapy has yielded very satisfactory results and constitutes the method of election for the treatment of carcinomas of the cervical stump.

Courtesy of References and Reviews
Journal of the American Medical Association

Sala, J., de Leon, A.: Radiology 81:300, 1963

TREATMENT OF PILONIDAL SINUS

At a U.S. Naval station hospital, comparison was made of hospital and outpatient surgical treatment of pilonidal abscess and sinus. This author found it entirely satisfactory to treat pilonidal abscess and sinus by local excision in the outpatient, packing the wound with gauze and then keeping the area cleansed and shaved, with dressings applied thereafter as indicated. He considered that the lesions healed in an average of 37 days and did not entail more than one day's disability from military service; and since the hospital-treated cases spent an average of 25 days in the hospital, he maintained that the outpatient treatment was just as effective as extended hospital care.

He speculated on the etiology of the disease, suggesting that the lesion develops as an infection around an ingrowing hair in the gluteal cleft, rather than as a congenital condition.

A bit more study in the etiology of this condition might have provided the author with considerable more enlightenment. In civilian practice it would be extremely rare to find a doctor who would confine his patient to the hospital for more than a day or two. However, as expense is apparently no criteria in a Naval hospital military regulations may require different procedures.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Kluge, David N.: Hospital Versus Out-Patient Treatment of Pilonidal Sinus. Surgery 57:245, 1965.

DIABETES AND TUBERCULOSIS

Patients with diabetes mellitus are more susceptible to tuberculosis and have more extensive disease. A review of 29 resections including 9 pneumonectomies and 6 segmentectomies, 2 decortications, and 3 primary thoracoplasties in 32 patients, indicated only a slightly increased morbidity and mortality rate over nondiabetic patients. Obesity is a common problem, especially in the Negro woman, making surgery and postoperative care more difficult. Management of the diabetes itself in the surgical period presented no specific complications. The diabetes was ameliorated postoperatively in 13 of the surviving 30 patients. Whereas four patients had preoperative spread of their disease, only one patient has had reactivation during the postoperative period up to 10 years, indicating the excellent postsurgical prognosis.

Courtesy of References and Reviews
Journal of the American Medical Association

Webb, W., Robinson, S., and Wofford, J.: Amer Rev Resp Dis 88:228, 1963

PORPHYRIA AND ANESTHESIA

In a patient with porphyria, even the most skilfully administered anesthetic may have a fatal outcome if it includes a barbiturate. No barbiturate should ever be given to a patient suspected of having porphyria. It is difficult to recognize this disease because it can simulate many other abdominal emergencies. When confronted with these emergencies, only an awareness of the disease and a knowledge of its intricacies will suggest the possible presence of this condition and lead to the testing of

Continued

urine for porphobilinogen. Porphyria represents a basic metabolic disturbance and appears in many forms. Two of these (intermittent porphyria and porphyria cutanea tarda hereditaria) both acute, are of importance to the anesthesiologist. The chelating agents have been used in the management of acute episodes with apparently good results, and this seems to be one of the most promising approaches for further study. The agents capable of precipitating an acute attack should be avoided such as the barbiturates, sulpha drugs, alcohol, heavy metals and oil-based paints, chloroquine, and progesterone. The over-all prognosis is poor. During an acute episode, the mortality rate in some series is as high as 50%. The future treatment of the disease may hold a large role for the anesthesiologist. Severe neurological involvement with respiratory failure may soon be treated in the respiratory unit and then, perhaps, the mortality rate can be lowered.

Courtesy of References and Reviews
Journal of the American Medical Association

Lepinskie, F.: Canad Anaesth Soc J 10:286, 1963

PTERYGIUM

A systematic sample of 463 veterans who had been operated upon for pterygium was compared to a similar sample of 19,000 veterans who sought medical and surgical care for any reason at Veterans Administration Hospitals. The relative frequency of veterans operated upon for pterygium increases as the latitude of the veterans' residence decreased. Rural veterans had a greater frequency of operation than urban veterans. Furmore, there was a significant association between U.S. Weather Bureau estimates of the ultraviolet radiation in sunlight in different parts of the United States, and the frequency with which rural veterans in these areas had pterygium operations. Ultraviolet radiation is proposed as an important environmental factor in the development of pterygium.

Courtesy of References and Reviews
Journal of the American Medical Association

Darrell, R., and Bachrach, C.: Arch Ophthal 70:158, 1963

Medicine

Medicine is both a science and an art . . . It is an art when it becomes necessary to apply it to a human being who is ill, and this is especially true when the manner of treatment is under consideration. It is in this art that the physician reveals how much talent he possesses; he reveals himself as a true artist by the particular form of remedial preparation which he decides to administer to his patient, by the felicitous choice which he makes between remedies, and by the favorable manner in which he combines them. — Armand Trousseau (1801-1867)

Natura sanat, medicus curat morbos; ne noceas, si prodesse credis. (Nature cures disease, the physician merely does what he can to facilitate the operations of nature; in your efforts to afford relief be careful not to do permanent harm.) — Christoph Hufeland (1762-1836)

Book Reviews

Books, the children of the brain.—Swift

MODERN NUTRITION IN HEALTH AND DISEASE, 3rd Edition — M. G. Wohl, M.D. and R. S. Goodhart, M.D. Lea and Febiger, Philadelphia, 1964. 1282 pages.

This book, written by 62 authorities in the field including physicians and basic scientists, presents a very broad and comprehensive discussion of nutrition and diet in health and disease. This 3rd edition has been completely revised and rewritten and includes some additional chapters on inborn errors of metabolism, nutrition in alcoholism and nutrition in neoplastic diseases. Part I of the book, which has 17 chapters, is devoted primarily to the basic physiology and biochemistry of nutrition. Part II is devoted to the clinical aspects of nutrition in disease, including an excellent chapter on the treatment of diabetes mellitus. Part III discusses nutrition in pregnancy, infancy and adolescence, in the aging person and during stress. Each chapter contains a number of tables and is followed by a very comprehensive bibliography. Although much of the book contains material on the physiologic aspects of nutrition, the entire text is oriented toward clinical medicine, and is easy to read and to use as a reference.

This text should be useful and of interest to internists, general practitioners, surgeons and pediatricians and will be a very valuable addition to the clinician's library.

Alvin L. Schultz, M.D.
Minneapolis, Minnesota

A DOCTOR DISCUSSES PREGNANCY — William G. Birch, M.D. with Dona Z. Meilach, Ph.D. Budlong Press Company, 1963. 110 pages.

This book is written in a very easy and understandable style and covers all aspects of prenatal care. It stresses particularly the relationship of the patient and her obstetrician. The responsibility of the husband and his understanding of the pregnancy is well outlined. This book is recommended for use in every physician's office who practices obstetrics. It will save him valuable time because so many common prenatal questions are so well answered. I have begun to use it in my practice.

N. M. Mensheha, M.D.
Minneapolis, Minnesota

SURGERY OF THE BREAST — Jorstad, Louis H., C. V. Mosby Co., St. Louis, 1964. Price $15, 220 pages.

This beautifully illustrated and well-bound journal, dealing exclusively with breast surgery, provides only a meager manuscript in its various chapters.

The first 12 chapters provide no eye-appealing headings or subheadings to induce the reader's attention and compel his interest. Very excellent line drawings probably need no more caption than is provided.

What the book lacks in organization it makes up for in illustrations, excellent binding, and high-grade printing.

For the surgeon interested in tumors of the breast, the monograph should be one of his possessions.

Carl O. Rice, M.D.
Minneapolis, Minnesota

DRUGS OF CHOICE 1964-65 — Walter Modell, M.D., Editor. The C. V. Mosby Company, St. Louis, 1018 pages, $16.75.

This is the fourth biennial edition of a book designed by its editor, a well-known Cornell pharmacologist, as a "practical guide to the selection of the best drug for a particular therapeutic problem." Each chapter is devoted to a particular therapeutic grouping, ranging from Drugs For Diseases of the Heart, through Drugs For Cancer and Allied Diseases, to Drugs For Children and "Anorexients." The difficulties of such a classification are obvious. That the attempt is brought off successfully is a tribute to the editorial skill of Dr. Modell and the composing ability of the forty-seven contributors, among whom are listed such familiar names as Bonica, Barach, Dameshek, Lasagna, Moyer and Karnofsky.

Each chapter is designed to be an expression of the opinion of the author, or authors, as to the relative merit of the drugs in current use in his, or their, field. There is too much "listing" of drugs.

Some of the discussion is excellent, concise, and useful, however, and the text is recommended for occasional reference or browsing.

Paul E. O'Brien, M.D.
Minneapolis, Minnesota

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Special Article

Rarity of Snakebites in Minnesota*

HENRY M. PARRISH, M.D., DR.P.H.**
Columbia, Missouri

MINNESOTA HAS the lowest U. S. incidence of poisonous snakebites west of the Mississippi River. Moreover, it has the fifth lowest snakebite rate for all states in this country (excluding Alaska and Hawaii). Those states with lower snakebite rates than Minnesota are all found in the New England Region. In keeping with this finding, there were no snakebite deaths in Minnesota during the 10-year period, 1950 through 1959.[1]

The purposes of this study are: (1) to chart the geographical distribution of poisonous snakebites in Minnesota; (2) to determine the annual incidence of snakebites; (3) to describe some medical and epidemiological characteristics of the bite accidents; and (4) to comment briefly on current concepts of snakebite treatment.

Poisonous Snakes

According to Klauber,[2] the following two species of poisonous snakes are indigenous to Minnesota: the timber rattlesnake (*Crotalus horridus horridus*) and the eastern massasauga (*Sistrurus catenatus catenatus*): a small rattlesnake. Both of these species are confined to the extreme southeastern part of Minnesota. Cottonmouth moccasins, copperheads, and coral snakes are not native to Minnesota. See Figure 1 for photographs of Minnesota's poisonous snakes.

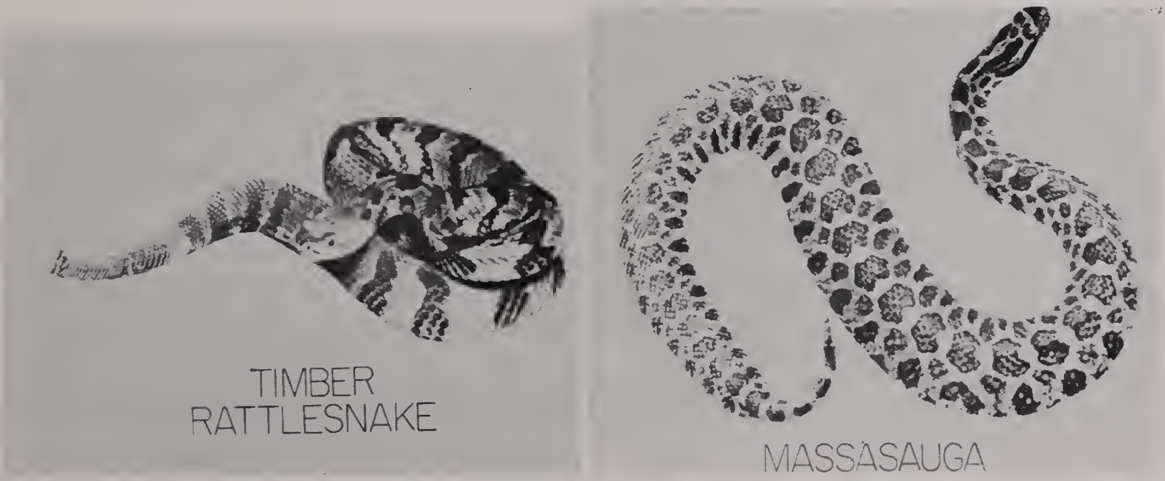

Fig. 1—Poisonous snakes indigenous to Minnesota. (Photograph of Massasauga Courtesy of L. M. Klauber, reference No. 2).

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*This investigation was supported in part by Public Health Service Research Grant GM 11268-02 from the Division of General Medical Sciences, Public Health Service.

**From the Department of Community Health and Medical Practice, School of Medicine, University of Missouri, Columbia, Missouri.

Continued

All of Minnesota's poisonous snakes are pit vipers, so named because of a characteristic pit which is located between the eye and nostril on each side of the body. Pit vipers are also identified by elliptical pupils and two well-developed fangs which protrude from the maxillae when the snake's mouth is opened. Rattlesnakes have rattles attached to their tails. Harmless snakes do not have facial pits; they have round rather than elliptical pupils, and while they have teeth, they lack fangs.

Frequently people chop off the head of a snake which has bitten someone and bring the snake's body in for identification. Pit vipers can be identified by turning the snake's belly upwards and noting a single row of subcaudal plates just below the anal plate. Harmless snakes have a double row of subcaudal plates. Figure 2 depicts the characteristic features of pit vipers and harmless snakes.

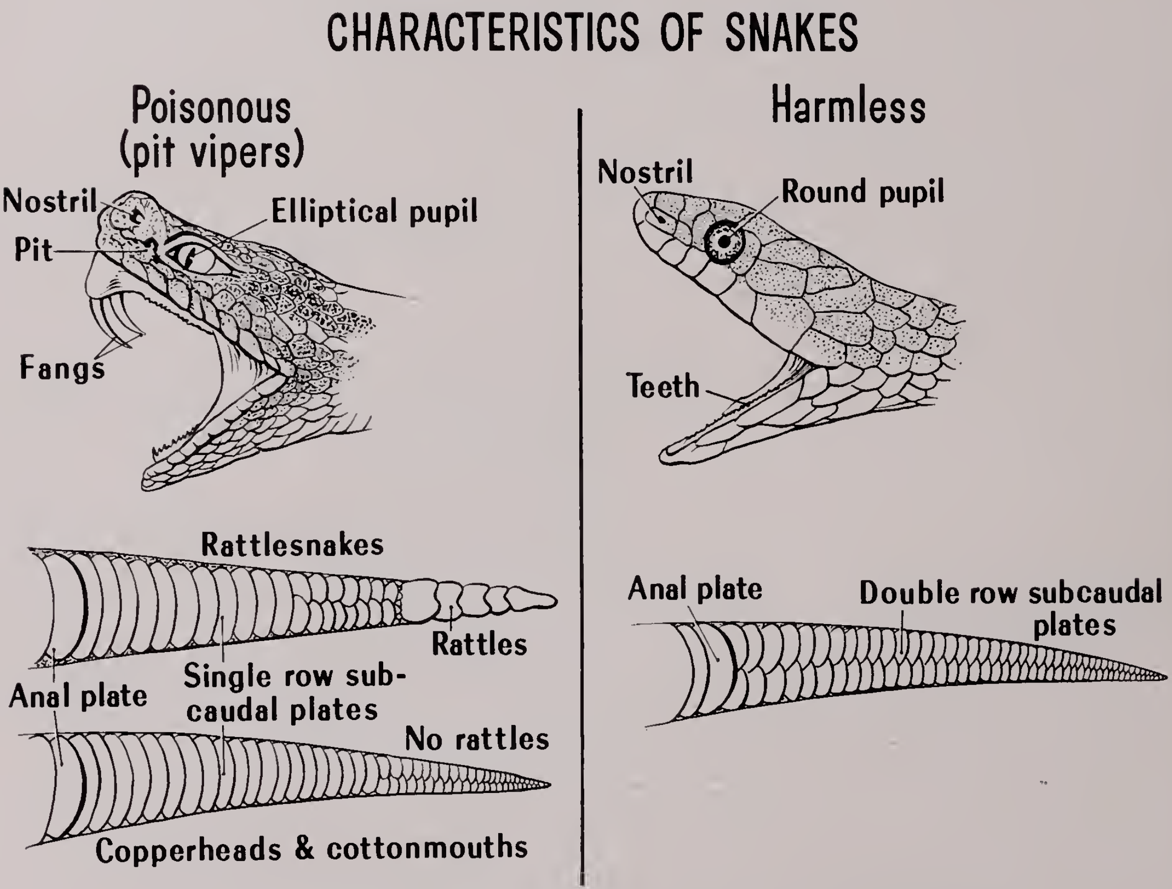
CHARACTERISTICS OF SNAKES
Poisonous (pit vipers)
Harmless
Nostril
Pit
Elliptical pupil
Fangs
Nostril
Round pupil
Teeth
Rattlesnakes
Rattles
Anal plate
Single row subcaudal plates
No rattles
Copperheads & cottonmouths
Anal plate
Double row subcaudal plates

Fig. 2—Characteristic features of poisonous (pit vipers) and harmless snakes.

Methods of Study

A questionnaire and letter explaining the purpose of this study were mailed to a "selected" group of Minnesota hospitals listed in Hospitals (Journal of the American Hospital Association) Guide Issue. Those selected for this study were general hospitals, children's hospitals, and college infirmaries. Army, Navy, Coast Guard, Public Health Service, Air Force and Veterans Administration hospitals also received questionnaires. Maternity, tuberculosis, and mental hospitals were omitted, as they would not be expected to treat snakebite victims. A total of 169 Minnesota hospitals comprised the study group. Each hospital was requested to report all inpatients admitted for snakebite treatment during 1958 and 1959.

Most hospitals do not code and tabulate the diagnosis of emergency room and outpatient clinic visits. Since some snakebite victims are not admitted to the hospital as inpatients, it seemed essential to ask a sample of practicing physicians how many snakebite victims they treated on both an outpatient and an inpatient basis. Previous surveys[3,4] have shown that most people with venomous snakebites are treated by general practitioners, surgeons, internists, pediatricians, or orthopedic surgeons. Therefore a random sample of one third of all the Minnesota physicians listed in these categories of practice in the A.M.A. American Medical Directory were sent questionnaires.

Death certificates for fatal snakebite cases were requested from the Minnesota Department of Health.

Results

This report is based on questionnaires returned by 169 Minnesota hospitals and is supplemented by questionnaires returned by 582 (81 per cent) of 715 practicing physicians in the State. The Minnesota Department of Health indicated that there were no snakebite deaths during 1958 and 1959.

Incidence

Minnesota hospitals reported a total of four inpatients treated for poisonous snakebites during 1958 and 1959, and *all of the analyses in this paper, excluding the estimate of incidence, were based on these four detailed case reports.*

On the basis of physicians' reports, when adjusted to account for all Minnesota physicians in the practice categories mentioned, it is estimated that approximately three people are treated annually for poisonous snakebites in Minnesota. This provides an incidence of 0.09 bites per 100,000 population per year.

Geopathology

The geographical distribution may be seen in Figure 3, the lightly shaded counties being those from which hospitals reported inpatients treated for snakebites.

Of four persons hospitalized for snakebite treatment for whom detailed records were available, two were bitten by rattlesnakes, one by a foreign snake, and one by an unidentified poisonous snake, most likely a rattlesnake. This bite occurred in one of the southeastern counties but was treated in St. Paul. A pet-shop worker was bitten by a foreign snake, an African rhinoceros viper (*Bitis nasicornis*).

Figure 3 shows that all of the snakebites occurred in southeastern Minnesota, showing the geographical patterns of bites to be consistent with the ecological ranges of poisonous snakes in Minnesota, as described by Klauber.[2]

Temporal Relationships

Snakebites were infrequent during the colder months of the year—Au-

Continued

gust through April, since snakes are usually inactive or hibernating during the colder months. The foreign snakebite, however, occurred in February. Of the bites by native snakes, one occurred in May, one in June, and one in July. The seasonal distribution of bites by native snakes coincides with the season when snakes are most abundant and active and when people undergo greater exposure due to out-of-doors occupations and recreation. Similar "seasonal epidemics" of venomous snakebites have been observed in New England and North Carolina.[3,4]

The times of day when the snakebite accidents occurred were: 9:00-11:59 A.M., one bite; 12:00 noon-2:59 P.M., two bites; 3:00-5:59 P.M., no bites; and 6:00-8:59 P.M., one bite. There were no bites from 9:00 P.M. through 8:59 A.M.

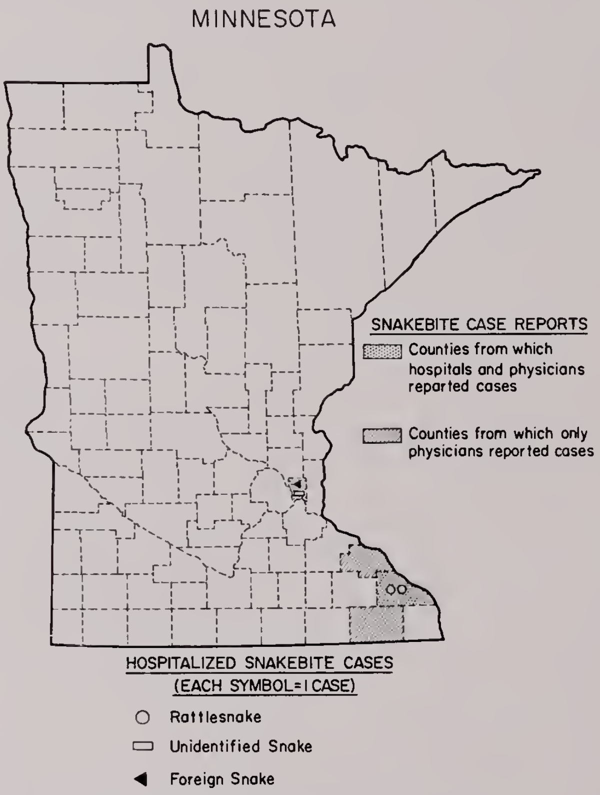
MINNESOTA
SNAKEBITE CASE REPORTS
▩ Counties from which hospitals and physicians reported cases
▭ Counties from which only physicians reported cases
HOSPITALIZED SNAKEBITE CASES (EACH SYMBOL=1 CASE)
○ Rattlesnake
▭ Unidentified Snake
◀ Foreign Snake

Fig. 3—Geographical distribution of poisonous snakebites in Minnesota, 1958 and 1959.

Bite Victims

There were three white males and one white female. Males usually have higher snakebite rates than females, and whites have higher rates than nonwhites.

Age and Sex

An analysis of the ages and occupations of the victims showed that one was a child, aged 12, one a housewife, aged 25, one a farm laborer, aged 63, and one a pet-shop worker, aged 34.

Two were bitten while handling a poisonous snake, one while picking berries in a field away from the house, and one while walking through a field away from the house.

Site and Severity

Two bites were on the fingers; the other two were on the lower extremities.

A modification of the clinical classification of pit-viper venenation* by Wood, Hoback and Green[5] was used to determine the severity of bites. Bites were classified as follows:

Grade 0—*No venenation.* Fang or tooth marks, minimal pain, less than 1 inch of surrounding edema and erythema. No systemic involvement.

Grade I—*Minimal venenation.* Fang or tooth marks, severe pain, 1-5 inches of surrounding edema and erythema in first 12 hours after bite. No systemic involvement usually present.

Grade II—*Moderate venenation.* Fang or tooth marks, severe pain, 6-12 inches of surrounding edema and erythema in first 12 hours after bite. Systemic involvement may be present—nausea, vomiting, giddiness, shock or neurotoxic symptoms.

Grade III—*Severe venenation.* Fang or tooth marks, severe pain, more than 12 inches of surrounding edema and erythema in first 12 hours after bite. Systemic involvement usually present as in Grade II.

There were no fatalities from snakebites in Minnesota from 1950 through 1959.[1] The case-fatality rate for snakebites in Minnesota is estimated to be less than one half of one per cent.

Treatment

A constricting band should be applied lightly to the involved extremity several inches proximal to the bite and only tight enough to occlude the superficial venous and lymphatic flow. *It should not occlude the arterial circulation* and it should be released every 10 to 15 minutes for a minute or two. As edema resulting from venom poisoning spreads, the constricting band should be advanced to keep just ahead of the swelling.

Incision-and-suction is effective in removing venom from experimental animals up to about 120 minutes after the venom is injected. The sooner it is used, the larger the amount of venom that can be removed. Suction should be used for about one hour. We have found the suction cups supplied in the Cutter and the Becton-Dickinson snakebite first-aid kits effective. Incisions, one-quarter inch long and one-eighth to one-quarter inch deep, are made into the subcutaneous tissues over the fang punctures. A few (3 to 5) additional incisions may be made in the surrounding edematous tissues, but a large number of incisions is not necessary. Immobilization aids in limiting the spread of venom; however, if one must decide between immobilization or seeking prompt medical treatment, the latter should be sought.

The "3 A's" (antivenin, antibiotics, and tetanus antitoxin and/or toxoid) are recommended, in addition to incision-and-suction, in treating all serious pit-viper bites. Antivenin Crotalidae Polyvalent (Wyeth) is effective in neutralizing the venoms of all North American pit vipers, but it is not protective against coral-snake venom. Since antivenin is manufactured from horse serum, the patient should receive a skin test before antivenin is given. For Grade I venenations antivenin may be adminis-

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*See Test Your Word Score Page 1029.

Continued

tered in the deltoid or gluteus muscles. In Grade II and Grade III venenations, antivenin diluted in 1000 cc. of normal saline may be given intravenously.[6] Studies with radioisotopes have shown that antivenin accumulates at the site of the bite more rapidly after intravenous administration than after intramuscular administration.[7] Injection of antivenin into the local bite area is not a particularly effective way to administer antivenin.

The following amounts of antivenin have been found useful in treating the various grades of venenation: Grade 0 requires no antivenin; Grade I may require 10 cc.; Grade II requires 30-40 cc.; and Grade III requires 50 cc. or more.

Since snakes' mouths and venoms may harbor pathogenic organisms, antibiotics and tetanus antitoxin and/or toxoid should be given prophylactically. Gram-negative organisms predominate; hence a broad spectrum antibiotic is indicated. Penicillin used by itself is not adequate treatment.

Antihistamines are contraindicated, as they shorten the survival time of animals poisoned with pit-viper venoms. Shock resulting from venom poisoning should be treated with infusions of blood, plasma, saline solution and vasopressor drugs. Meperidine hydrochloride and other analgesics may be given to relieve pain. Recently there have been reports of excessive tissue necrosis and amputations associated with cold therapy, such as packing an extremity in ice or using ethyl chloride.[8] In my opinion, cold therapy should not be used in treating pit-viper bites.

Summary

Poisonous snakebites rarely occur in Minnesota. An estimated three people are bitten annually, which provides an incidence of 0.09 bites per 100,000 people. The case-fatality rate is estimated to be less than one half of one per cent.

Most of the reported bites occurred in southeastern Minnesota from May to August. Of four bites reported in detail, two were inflicted by rattlesnakes, one by a foreign snake, and one by an unidentified snake. All of the bites were on the extremities.

The treatment recommended included incision and suction and the administration of antivenin, antibiotics and antitetanus prophylaxis.

Acknowledgement: The author cites with gratitude the technical assistance of the following persons: Linda Hinson, Judi Pummill, and Genevieve Calescibetta.

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7. McCollough, N. C., and Gennaro, J. F., Jr.: Evaluation of Venomous Snake Bite in the Southern United States From Parallel Clinical and Laboratory Investigations: Development of Treatment. J Florida Med Assn 49:959, 1963.

It takes less time to do a thing right than it does to explain why you did it wrong.
— Longfellow

Perinatal Mortality Study

Fetal Death During Labor*

Case Report

The mother of this infant was 27 years old and Rh positive; she had had no difficulty with the present third pregnancy or with her other two pregnancies. Both of her children are living and well.

At 38 weeks of gestation she spontaneously went into labor and entered the hospital after six hours of labor. At this time her blood pressure was 120/80, fetal heart rate 140 per minute and fetal station minus 2. Although the mother continued to have mild contractions, she had no further examinations or check of fetal heart rate until six hours after admission (12 hours after onset of labor), at which time the uterus was very tense, the cervix 2 cm. dilated and fetal station minus 1, and the fetal heart tones absent. The mother's physician was called; he did a sterile vaginal examination 45 minutes later and made the diagnosis of possible abruptio placenta. The membranes ruptured one hour later (blood pressure recorded second time since admission — 120/80).

A stillborn infant weighing seven pounds, four ounces was born 12 hours after admission. No autopsy was done. The placenta, which immediately followed the infant, was covered with numerous blood clots. Following delivery, the mother's hemoglobin was 8.9 gm.%. (The hemoglobin had not been checked before delivery; it was 74 to 80 per cent during pregnancy.) The mother's fibrinogen level following delivery was 75 to 125, which was considered borderline. She received one pint of blood, which raised the hemoglobin to 10.1 gm.%.

Comment

The Ramsey County Perinatal Mortality Study Committee criticized the care which this mother received while in labor. As long as the mother continued to have mild contractions, there should have been a check of her blood pressure and fetal heart rate at least once each hour. Blood pressure, rectal examinations of the cervix and fetal heart-rate determinations should be done and recorded at least every 30 minutes during active labor in multiparous patients. Hemoglobin should be done on admission.

Although more frequent listening and recording of the fetal heart rate may not have made a difference in the final outcome in the present case, possibly there might have been a marked drop in the fetal heart rate before it ceased altogether. With this drop, measures could have been carried out to deliver this full-sized infant before it expired. The Committee will continue to study perinatal deaths and attempt to find factors, the use of which may salvage some of these infants.

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*Ramsey County Perinatal Mortality Study Committee.

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— Helen MacIntosh, N. E. A. Journal

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The Medical Evaluation of Physical Disability in the Employee

S. CHARLES FRANCO, M.D.*
New York, N. Y.

IN INDUSTRY the evaluation of disability is important in a variety of conditions involving extended sick absence, physical impairment, and behavior problems. It consists of rating the physical or mental impairment so that an appraisal of the employee's ability to engage in gainful and productive work can be determined.

At Consolidated Edison, the function of the medical department in the disability evaluation program is to obtain specific diagnostic information that will be useful in guiding management in reaching a proper administrative decision. The confidentiality of medical records must also be maintained.

Disability Panel

The disability panel is composed of representatives from the personnel department (the personnel director acts as chairman) and the medical department, a supervisor from the employee's department and a representative from the executive level of management. If the employee's disability is the result of occupational injury or disease, a member of a company's insurance bureau also attends the meeting.

The panel procedure consists of a weekly meeting to consider the cases presented to it by the departments. Its evaluations and recommendations as to disposition of cases are based on factors such as the medical report, the worker's service record, his attendance and job performance records, and his status with regard to disability under the union agreement.

The report covers the employee's attitude, job performance, and absence record. The whole problem is then discussed by the panel; but the primary responsibility for decision rests with the department concerned. In the event of a failure to reach a

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*Executive Director of the Medical Department, Consolidated Edison Company of New York, Inc.

Continued

decision the problem is then reviewed by the vice president of the department concerned.

It was revealed that the majority of cases reviewed at Consolidated Edison were over 45 years of age with more than 25 years of service. The 10 most common disabling diseases were:

	No. Employees	%
Cardiovascular disease (coronary disease-171)	230	(32.6)
Functional nervous disorders (psychoses-60)	140	(19.8)
Cancer	55	(7.8)
Fracture	37	(5.2)
Arthritis	26	(3.6)
Peptic ulcer	20	(2.8)
Herniated intervertebral disc	15	(2.1)
Cerebral vascular disease	13	(1.8)
Chronic bronchitis and emphysema	13	(1.8)
Cirrhosis of liver	12	(1.7)

Multiple Disease

As is common in an older age group, a fair percentage were affected by more than one disease. Further scrutiny of the cardiovascular disease system indicates that coronary artery disease accounts for 75% of the disabling conditions. The complications of hypertension account for most of the hypertensive vascular disease. The relative infrequency of rheumatic heart disease is also reflected in the statistics.

Functional Disorders

Functional disease of the central nervous system is the second most prevalent condition. The psychoses were usually identified by a medical report of sick absence from a physician. At times abnormal behavior on the job provided the first signs to supervisors, and a medical referral to the diagnostic clinic was obtained on an emergency basis. As would be expected in an older age group, affective psychosis accounted for 75% of the cases. A change in personality, increased sick absence, and deteriorating job performance were often clues in the neuroses. The anxiety neuroses were frequently associated with medical complaints. Outside neuropsychiatric consultation is obtained in all cases for guidance and recommendation.

Fifty Percent Re-Employable

A review of the functional nervous disorders (Table 4) indicates that approximately 50% of the employees were returned to duty. The over-all attendance record, previous occurrences of psychiatric disorders, and the department's evaluation of work performance were important factors in the consideration for approval to return to work. Retirement was most often recommended in cases with recurrent episodes, excessive sick absence, and deteriorating work performance. By and large the subsequent work experience of the recovered neuropsychiatric case has been satisfactory. Physically restricted duty was required in a little more than one third of the cases, usually with reference to the responsibility for safety of others in certain hazardous job operations. At times, some recovered psychotics were restricted to job activity under close supervision.

Alcoholism

A majority of the alcohol problems (75%) were reviewed. Some had availed themselves of therapy, but nearly 25% were identified by medical examination as revealing the chronic sequelae of organic disease, such as cirrhosis, polyneuritis beriberi and malnutrition.

Retirement Recommended

Retirement was recommended in 85% of the cases of alcoholism reviewed by the panel. Many employees were considered for recurrence of drinking episodes under the procedure on alcoholism; a number of these had not followed any type of medical therapy. Others had not been identified under the company procedure on alcoholism, and their recognition at an advanced stage of the disease made any attempt at rehabilitation unrewarding. By contrast, the long-term experience under the procedure on alcoholism with employees who had followed the recommended treatment has shown a 60-percent rehabilitation rate.

Cardiovascular Disease

A more detailed analysis of the cardiovascular disease cases is rendered in Table 1. Of those who survived the acute attack of coronary thrombosis, 56% returned to productive work.

Sick Absence

Sick absence constitutes a major problem. Any sick absence extending beyond five days requires examination in the medical department before return to duty can be approved.

The medical reports of all cases of sick absence extending beyond two weeks are promptly reviewed by the medical department to establish the cause of illness. Periodic re-evaluation of follow-up reports is scheduled at intervals based on the nature of the underlying disease. In addition to the usual channels of communication with the attending physician, evaluation based on physical examination in the medical department or at home may be required. Hospital cases are usually deferred until the convalescent period has been completed. Under company procedure sick absence extending beyond eight weeks requires review by the disability panel.

Medical administrative opinion should be based on good clinical practice rather than on "book rule." The industrial physician has a moral obligation to consider the employee's rights to his job as well as his physical welfare.

Cardiovascular Disease

Limited Activity

Most of the cases of cardiovascular disease will require limitation on heavy lifting and repeated stair climbing and, in severe cardiacs, walking or continuous standing may have to be curtailed.

Angina Pectoris

Employees with angina pectoris or convalescent from acute coronary thrombosis should not be assigned to jobs in which the sudden occurrence of symptoms would endanger the safety of others. They should not drive motor vehicles.

Asymptomatic Coronary Disease

The asymptomatic employee with coronary thrombosis can return to physically restricted work three to four months after his acute episode. The asymptomatic patient with a stable electrocardiogram may be permitted to drive light vehicles at the end of one year after an acute episode. There are some who have recommended that the asymptomatic coronary thrombosis case can return to "his former work" even at a rela-

TABLE I

Final Disposition of Cases Reviewed by Disability Panel, According to Primary Condition

Diagnosis	Total Cases	Released	Full Duty	Physically Restricted Duty	Separation Allowance	Retired	Deceased
Cardiovascular Disease							
Coronary thrombosis, acute	118*	2	3	64	15	33	1
Coronary thrombosis, old	3			2		1	
Arteriosclerotic heart disease	49†			11		38	
Angina pectoris	1					1	
Total	171	2	3	77	15	73	1
Functional Nervous Disorders							
Anxiety neurosis	37	1	14	5	3	14	
Chronic alcoholism	35		5		1	29	
Psychosis	60	2	23	9	9	17	
Psychoneurosis	8					8	
Total	140	3	42	14	13	68	

*Survived acute attack.
†Over-age cases (65-68 years).

Continued

tively heavy job. We are impressed by the adverse effect on industrial relations when the "recovered coronary" has a recurrence or dies on the job. We also have seen the untoward effect of heavy physical work on the recent coronary thrombosis patient. In the past 15 years, recurrences on the job have been practically nonexistent in our physically restricted coronary disease group. There has been only one claim made under compensation since 1950 and this was rejected by the Workmen's Compensation Board.

The coronary artery disease patient who has made a complete clinical recovery may be considered for full duty after a two-year follow-up. The asymptomatic individual with normal blood pressure, and normal cardiac size, without diabetes, and with a normal, double 2-step exercise electrocardiogram test can be considered for return to full duty without physical restrictions. Unfortunately this number is relatively small and comprises less than 5% of the cases of coronary thrombosis.

Hypertension

Cases of essential hypertension, with blood pressure levels up to 180/100, usually will not require physical restrictions. However, every clinical precaution should be taken to uncover latent coronary disease.

Persons with rheumatic heart disease, who have not experienced congestive failure, can perform surprising amounts of physical exertion without obvious detrimental effects. Aortic valvular disease usually poses more problems than mitral involvement.

Arthritis, Back Disorders, and Discogenic Disease

Avoidance of work assignment in wet or damp locations or in sustained low temperatures is important in the medical management of the arthritic employee.

Osteoarthritic joints with definite degenerative changes should be spared further trauma as well as additional wear and tear. However, one should avoid the pitfall of hypertrophic spurs on the bodies of spinal vertebrae without other distinction.

Depending on the location of the arthritic condition, work in certain cramped positions should be avoided.

An employee with a functional type of back complaint may make a rather remarkable improvement when his job is placed in jeopardy. It would be wise for the physician to document carefully the employee's reaction to various work assignment when there is an absence of limiting clinical findings to confirm an organic back complaint.

It has been our experience that preemployment x-ray films of the spine often do not identify potential back conditions. Herniated disc is the most common back condition, and the vast majority of patients with it show normal x-ray films.

A well-motivated employee, after operation for herniated disc, can often resume heavy work despite the recognized anatomical alteration in the spine.

Pulmonary Disease

In cases of healed pulmonary tuberculosis, nonspecific pulmonary fibrosis, chronic bronchitis, emphysema, and asthma, patients require a protected work atmosphere as regards dust, dampness, changing temperature, and extremes of temperature.

It has been a common clinical experience that spontaneous pneumothorax rarely recurs after a six-month interval, and it is not practical to continue physical restrictions on heavy lifting beyond that time.

Neurological Disorders, Epilepsy, Syncope, and Vertigo

Cerebral thrombosis constitutes the largest proportion of this group. In the absence of hypertension, the cerebral thrombosis cases may be rehabilitated to a surprising level of work performance. Evaluation of permanent impairment should be deferred until maximum rehabilitation has been achieved, which may take up to six months. Nevertheless, employees who have had cerebral thrombosis will continue to require certain physical restrictions to protect them against unusual strain and working in hazardous situations. Recurrence of vascular episodes can be expected in a four-year period[5] in 50%.

Subarachnoid hemorrhage, on the other hand, imposes a continuing hazard even at protected jobs.

Convulsive Seizures

Persons with convulsive seizures require careful neurological survey, including at least an electroencephalogram to determine, if possible, the etiological factor. In some cases it may be wise to perform cerebral angiography and pneumoencephalograms. Syncopal episodes under severe functional stress should not be the cause for precipitous application of physical restrictions of a permanent nature. Obviously, the epileptic should work in a protected environment and should not be responsible for the safety of others. A hidden alcoholism problem may also manifest itself by convulsive seizures.

Vertigo

Functional vertigo raises many problems. Reassurance of the employee by a complete medical work-up can serve to eliminate a certain percentage of these cases from serious consideration.

Persons with multiple sclerosis and amyotrophic sclerosis involving disability of locomotion can be placed at sedentary work. However, involvement of the upper extremities may pose a serious disability. The progressive nature of these conditions requires careful periodic re-evaluation.

Neuropsychiatric Problems

Persons with anxiety neurosis, psychosomatic disturbances, and reactive depression may make a good response to treatment and are capable of productive work.

More persistent problems arise with psychoneurosis, recurrent depressive psychosis, and schizophrenia. Such individuals may not be able to carry the full responsibility in an operating job assignment in a public utility. They may require work under close supervision.

The suicide risk, even when recovered, needs close supervision at work for a varying period.

Borderline Personality

Persons with a borderline personality, functioning between normal and pathological, may present abnormal behavior on the job, poor work performance, and increased absenteeism, and may show very few clinical findings. The disposition of these problems is often administrative because the medical department may not be able to identify any legitimate underlying medical or psychiatric condition.

Diabetes Mellitus

The mild controlled diabetic, even one who takes small amounts of insulin (up to 10 units N.P.H.), may not require physical restrictions.

Driving Hazard

Where there is danger of insulin shock, the employee should be limited with respect to driving and hazardous work. In the matter of driving motor vehicles, the diabetic who requires insulin is excluded from truck driving, but those whose insulin dosage is moderate (up to 40 units of N.P.H.) may be able to drive passenger vehicles.

The "brittle" diabetic whose control is difficult should avoid shift work, particularly the "graveyard" shift from midnight to 8 A.M.

In the presence of organic complications, such as peripheral arterial disease, cardiac, or renal involvement, appropriate protective measures must be taken.

Abdominal Conditions

We use this category to cover a variety of gastrointestinal and genitourinary diseases.

Chronic peptic ulcer symptoms may be disabling enough to require elimination of shift work. The complications of peptic ulcer may be considered as an indication for surgical intervention.

The relationship of colon disorders to psychosomatic disturbances is well known.

Summary

The medical evaluation of physical disability is the key to the safe and productive employment of the physically impaired worker. It is the firm basis for selective placement at a suitable job. Follow-up by periodic medical evaluation is also an important factor in keeping the handicapped employee on the job without harm to himself.

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Medicine and Religion

The Physician and Reality Therapy

ELOF G. NELSON, S.T.M.*
Minneapolis, Minnesota

Reality is the concrete embodiment of truth. All dimensions of reality are germane to the physician's management of the whole person. To ignore the patient's spirit and the manifestations of that spirit in religio-social living is as incomprehensible as ignoring the patient's vascular system. We need to begin asking people: "What makes you tick?"

Everything about this space age in which we live has exciting possibilities for good as well as for evil. Our dynamic culture, filled with the fruits of the Industrial Revolution, scientific progress and its concomitant socio-economic bonanza, points to a negative as well as a positive outcome.

Our houses, offices, bank accounts and leisure activities reflect the many "assets" of space-age living. We have more things to make us happy than any generation in all human history; however, we are neither a happier nor a more grateful generation. The more man has, the more he seems to live on the edge of poverty with a thousand needs and wants.

We are all rather familiar with the facts — or symptoms, if you wish to think of them in clinical perspective. I shall not enumerate here the sociological and cultural trends of our time. Anyone who spends his daily life treating people has long since collected his own clinical evidence.

Success is a difficult reality factor to live with. American people apparently are not genotypically capable of living with it. Far too many are incapacitated by psychic pain resulting from the stresses of life, because they simply do not know how to adjust to a "successful culture." Many of your patients live in an existential vacuum; they are neither pilgrims nor tourists, but wanderers.

People are stunned by this turbulent culture. They feel the whirling pace around them filling them with anxiety, frustration, and conflict. Nothing makes sense, and they drift into many kinds of unrealistic thought, affect and activity. We note a deluge of symptoms: boredom, loneliness, spiritual malaise, purposelessness, psychosomatic illness and the many neuroses.

Sick Societies Produce Sick People

Reality has always impinged on human life with anguish and pain. As T. S. Elliot says, "We can't stand reality very long." We are becoming masters of self-deception and we find it increasingly convenient to project responsibility to other persons or things. Not many people can stand the truth about themselves and their obligation as mature persons of meeting life's crises and demands in a rapidly changing world. Vast numbers of people are escaping into illness and apathy.

American culture seems to be saying that the aim of life is to avoid facing up to reality and to attain happiness by any means desirable. We are on a massive "happiness kick"; we must not deny ourselves anything; what we want, we ought to have here and now. We have become a culture which has begun to scorn the old patriarchal values of decency, honesty, loyalty, honor, and integrity. People no longer know who they are, as one scene from "Death of a Salesman" vividly illustrates. The words were uttered by Willie's

Continued

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*Director, Department of Religion & Health, Fairview Hospital.

own son at the graveside: "The trouble with Willie was that he never knew who he was." Depersonalized man is a strong candidate for physical, emotional or moral suffering. Perhaps, therefore, life's greatest tragedy is not that people die — but that some people never learn how to live.

Help People Test All of Reality

For many people, their psychic metabolism is out of gear and life meaningless. They are suffering from a "philosophical neurosis," all too evident in such physical findings as fatigue, and psychosomatic aches and pains, as well as in all types of addictions and escapes from reality.

Religion too has become a dull habit, something to exploit rather than to live. In American life today, there is great religious exposure but little religious commitment; people are submitting to the values of faith but there appears to be little surrender. If we take a moment of time to analyze people, we discover that they have a distorted world view and exist in a vacuum of philosophical poverty. They are spiritually bankrupt.

Individuals expect their God to be a great White Father, something like Santa, who doles out jobs and promotions, assures optimum working conditions for all, and provides bulging bellies, fast cars, and plenty of playthings for week-end pleasure.

The seven deadly sins of pride, envy, anger, sloth, avarice, gluttony and lust are spiritual cancers which daily take their toll in our patients' lives and may well be greater factors in the practice of medicine today than ever before in its history.

Patients often feel a relationship of trust toward their physicians; perhaps no one else but the physician can so relate to the patient. Pastors in larger metropolitan areas have neither the time nor the training to counsel; and often people in these communities are reluctant to relate to their pastor on a personal, subjective level.

Suggestions for Management

Physicians would do well to manage the whole person by thinking in terms of social-religious living as well as organic-physiological constructs. Helping people to face total reality, not excluding the spirit of a man: this I would call reality therapy. In this therapy the physician should involve himself in a teaching role; he should challenge, modify or correct behavior, thought, feelings and motives arising from the soul of man.

The following steps may give you new "pastoral tools" to aid in facilitating treatment of the whole person:

A. Ask:
  1. Are you content with yourself?
  2. Are you getting along with others reasonably well?
  3. Are you accepting responsibility for your mistakes and success in life?
  4. Are you living a good life — are you *sure* you know right from wrong?
  5. What are you living for — what is the central, controlling idea in your life?
  6. Is that central, controlling idea big enough to live well for — is it worthwhile dying for?

B. Emphasize the person's condition as weakness or indifference, *not* illness.

C. Point out that weakness can be strengthened by:
  1. Meeting life's responsibilities daily.
  2. Confronting, *not* evading life's conflicts and disappointments — thus developing moral and ethical consciousness.
  3. Understanding the nature of love: learning to give and receive love.
  4. Placing positive values on the focal points of reality about which we all feel ambivalence: Birth, Death, Love, Sin, Illness, Crisis.
  5. Living the seven virtues: Wisdom, Justice, Courage, Temperance, Faith, Hope, Love.

Man cannot live by bread alone. As you challenge, modify or change people's style of living by giving meaning, purpose and commitment to life, you will stand people on their feet.

There is nothing so well known as that we should not expect something for nothing — but we all do and call it Hope. — E. W. Howe

History of Medicine

Joseph Lister (1827-1912)

> *It was his part to learn of the power of Medicine and of the manner of healing and, heedless of glory, to exercise that quiet art.*
> —*Virgil, Aeneid xii, 396-7*

This year we celebrate the centenary of the first successful case treated antiseptically by Lister, who is inseparably linked with the history of antiseptic surgery.

The frightful mortality in the years before "Listerism" . . . "was the burden of all military surgery, all hospital and private practice, all midwifery, in every city on earth, for centuries. Pyaemia, septicaemia, erysipelas, cellulitis, hospital gangrene . . . we have only to note that these infections were scourging the Glasgow Infirmary, to their hearts' content, right up to 1865, as they were scourging other hospitals in all countries; and were called . . . hospital diseases."[1]

Joseph Lister was brought up in the tranquil, unpretentious atmosphere of a Quaker family. His father, Joseph Jackson Lister, a man of remarkable attainments, gave his leisure time to microscopic studies. To his investigations we owe the production of the achromatic lens and the perfection of the modern telescope. The Quaker abstention from more worldly amusements also provided the incentive to young Lister to pursue natural history studies and read the Latin classics. He announced when very young his intentions of becoming a surgeon. Studying at University College, London, Lister came under the influence of two exceptional professors, Wharton Jones and William Sharpey. From Jones, who had made important discoveries in physiology, Lister began to study the circulation and the effects in inflammation on the web of the frog's foot. During the years he spent as a Resident Doctor at University Hospital he joined with a brilliant group of young enthusiasts in the Hospital Medical Society, conducting research and reading original papers. Lister's papers on "Gangrene" and "Observation on the Muscular Tissue of the Skin" indicated the direction in which his mind was working.

Upon the advice of Professor Sharpey to visit Edinburgh to observe some of their methods, Lister went in 1853. Soon he was asked by Dr. James Syme, Professor of Clinical Surgery at Edinburgh University to be his assistant in his private practice as well as at the Royal Free Infirmary. Syme was one of the great surgeons of his day. Under his tutelage Lister matured as a surgeon and also carried out important research concerning inflammation and blood coagulation. Their compatible professional relationship was enhanced by the marriage of Lister to Agnes Syme, Doctor Syme's eldest daughter. At his post as Assistant Surgeoncy at the Infirmary, Lister continued his researches into the causes and exact nature of inflammation.

In 1860 he was appointed to be Professor of Surgery at the University of Glasgow and Surgeon at the Royal Infirmary. By 1865 he had done a vast amount of scientific work on the subject of inflammation. Seeking a solution to the problem of wound infections, Lister became interested in Pasteur's work. Now that the French chemist had shown that decom-

Continued

position was due not to the air but to the living organisms carried by particles of dust in the air, Lister decided to try to prevent infection by excluding the air from wounds with a dressing containing a material potent enough to destroy the floating particles. ". . . to apply some chemical substance in such a manner that not only would the microbes already present be destroyed, but the germ-killing substance must act as a barrier between the wound and all sources of outside infection."[2] He used as his first antiseptic agent full strength carbolic acid, which under the name of German creosote, was supplied to him by his colleague, Dr. Thomas Anderson.

His first successful case to test his new principles was that of an eleven-year-old boy admitted to the Glasgow Royal Infirmary on August 12, 1865, suffering from a compound fracture of the left leg caused by the wheel of a cart passing over the limb a little below the middle. "A piece of lint soaked in the undiluted carbolic acid was applied to the wound, after which the limb was padded and placed in the usual splints. The limb was left undisturbed for four days. . . . Lister found, to his joy, that there was no sign of suppuration in the wound."[3]

With profound care and watchfulness he progressed from case to case, modifying his first method as he found that a dilution of the acid was sufficient to effect asepsis in wounds. His carbolic acid spray, sometimes called the "Donkey machine" was with him at every operation for many years, altho it did produce irritating vapors.

He introduced the catgut ligature and was constantly experimenting and improving it. "Lister prophesied that it would be possible to tie arteries in their continuity in cases of aneurism, and that it would be no longer dangerous to ligature an artery close to the emergence of a large branch. Before applying these ideas to the human subject, he experimented upon an old horse on December 12, 1867. The horse made an excellent recovery. Indeed, its condition improved greatly under the good feeding and management of the veterinary establishment, but in five and a half weeks it died from old age. Lister, who made a post-mortem examination, found his expectations fulfilled. Not only had the artery been successfully occluded, but the ligature had been surrounded by strong fibrous tissue, and there were no signs of pus, granulations or softening of the tissues."[4]

"As the years passed by it became recognized, both by the profession and the public, that he was the greatest surgeon the century had produced, and honors, British and foreign, were showered thickly upon him. . . . Long before he died he had become a national hero, and an object of world-wide respect."[5]

The name of Joseph Lister will ever be honored and venerated as one of the greatest benefactors of the human race. The results of his manifold labors may be summed up in a phrase: he made surgery clean.

References

1. Paget, Stephen: Pasteur and After Pasteur, Adam and Charles Black, London, 1914, p. 33.
2. Dukes, Cuthbert: Lord Lister, Leonard Parsons, London, 1924, p. 90, 91, 107, 165.

Happy is he who has been able to learn the causes of things.— Virgil 70 B.C.

Meetings and Announcements

Free and fair discussion will ever be found the firmest friend to truth.
— *G. Campbell*

AUGUST

Southern Minnesota Academy of General Practice, Seminar, 3:45 p.m., August 24, LeSueur.

University of Wisconsin Medical Center three-day course on ongoing developments in surgery, August 26-28, at the Medical Center. Contact: Paul Knipping, 401 Extension Bldg., University of Wisconsin, Madison, Wisconsin.

American Academy of Physical Medicine and Rehabilitation, August 22-27, at the Sheraton Hotel, in Philadelphia. Contact: The Academy at 30 North Michigan Avenue, Chicago.

American Physicians Fellowship orthopedic seminar, August 4-15, in Israel. Contact: American Physicians Fellowship, 1622 Beacon Street, Brookline, Mass.

SEPTEMBER

Zumbro Valley Medical Society, September 1, Plummer Hall, Mayo Clinic, Rochester.

St. Louis Co. Medical Society, Executive Comm., September 9, 6:00 p.m., St. Mary's Hospital, Duluth and Regular Meeting, 8:00 p.m.

Minnesota Heart Association, Annual Meeting, Scientific Sessions, September 18, 9:00 a.m. — 5:00 p.m. (Place unknown).

Minnesota Medical Foundation, Annual Meeting, September 27, 8:00 p.m., Mayo Auditorium, University of Minnesota, Minneapolis.

Minn. Academy of General Practice, House of Delegates, 4:00 p.m., September 28, Hotel Radisson, Minneapolis.

Minn. Academy of General Practice, Fall Refresher, Radisson Hotel, September 29-30, Minneapolis.

Ramsey Co. Medical Society, Business Meeting, 8:00 p.m., 15th Floor Lowry Medical Arts Bldg., St. Paul, "Nominations for Officers," September 27.

Annual West North-Central Interprofessional Seminar on Diseases Common to Animals and Men, University Hospital in Iowa City, Iowa, on September 16-17. Contact: Dr. W. F. McCulloch, Institute of Agricultural Medicine, University of Iowa, Iowa City.

Southern Minnesota Medical Association Meeting at the Sheraton-Ritz Hotel in Minneapolis, September 10th. Contact: John Eustermann, M.D., Mankato Clinic, Mankato, Minnesota.

Department of Otolaryngology, College of Medicine of the University of Illinois at the Medical Center, Chicago, will conduct a postgraduate course in laryngology and bronchoesophagology September 20-October 2. Write: University of Illinois Medical Center, Post Office Box 6998, Chicago 60680.

Seventh Annual Methodist Hospital Symposium — Methodist Hospital in Minneapolis. September 11th.

Fall Meeting of Minnesota Radiological Society, Ruttger's Lodge, Brainerd, September 11. Carman Lecturer will be Dr. Harold Jacobson of Montefiore Hospital, New York City. Contact: E. A. Peterson, M.D., 572 Lowry Medical Arts, St. Paul.

OCTOBER

American Fracture Association Meeting, Las Vegas, Nevada on October 24-28. Contact: W. Compere Basom, M.D., 1220 N. Stanton St., El Paso, Texas 79902.

Annual Meeting of the Academy of Psychosomatic Medicine, October 11-13, Sherman House, Chicago. Edwin Dunlop, M.D., 150 Emory St., Attleboro, Mass. 02703.

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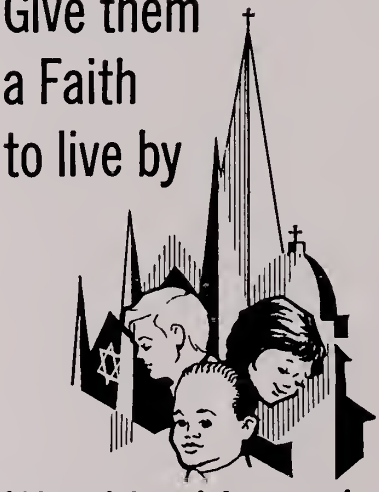

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MEETINGS AND ANNOUNCEMENTS

Annual Course in Postgraduate Gastroenterology of the American College of Gastroenterology, Americana Hotel in Bal Harbour, Florida, October 28, 29, 30. Contact: College, 33 West 60th Street, New York, N. Y. 10023

American College of Nutrition Annual Scientific Meeting, Americana Hotel in New York City, October 10th. Contact: R. A. Peterman, M.D., 3 Craig Court, Totowa Borough, New Jersey 07512.

American Academy of Pediatrics 34th Annual Meeting, October 23-28, Palmer House, Chicago. Write: Academy, 1801 Hinman Avenue, Evanston, Illinois.

ANNOUNCEMENTS

Hahnemann Medical College & Hospital, Philadelphia, postgraduate courses:
Nov. 22-24 — Symposium Cancer Chemotherapy, Sheraton Hotel.

* * *

Three-day course directed to surgically oriented physician will be held at the University of Wisconsin's Medical Center, Aug. 26-28. Aspects of cardiovascular surgery, biliary tract surgery, and general abdominal surgery will be presented. Write: The University in Madison.

* * *

A nine month tutorial program in Cardiology, September 15, 1965 to June 15, 1966, will be offered by Institute for Cardio-Pulmonary Diseases, Scripps Clinic and Research Foundation, La Jolla, California. For details: Write E. Grey Diamond, M.D., Scripps Clinic and Research Foundation, La Jolla, California.

* * *

The University of Minnesota Department of Pediatrics continuation course in pediatrics, September 21-23, University of Minnesota Campus in Minneapolis. "Genesis, Epigenesis, Modern Physic and the Child" is the subject. Contact: Edward Defoe, Department of Pediatrics, University of Minnesota Hospitals, Minneapolis 55455.

* * *

Three day meeting in Cardiology at the Lowry Hotel, St. Paul, September 15-17, under the sponsorship of the Council on Clinical Cardiology of the American Heart Association, the St. Paul Medical Center, and the Minnesota Heart Association.

The focus of this three-day postgraduate course will be on functional pathology of valvular and pericardial diseases — congenital and acquired types.

The course will be directed by Jesse E. Edwards, M.D., Director of Laboratories at Charles T. Miller Hospital and board member of the American Heart Association. Doctors Lewis S. Carey, Robert S. Eliot, James N. Karnegis and James Ronan will be on the faculty.

The Blue Shield

Blue Shield Will Occupy New Minneapolis Office

Blue Shield of Minnesota, the state's largest medical-surgical plan, has announced its purchase of a new headquarters building at 2344 Nicollet Avenue, Minneapolis.

Thomas C. Paton, executive vice president, said the medical service organization plans to occupy the four-story building as its state headquarters July 26, 1965.

Paton said that Blue Shield's present offices at 2218 University Avenue, on the Midway in Saint Paul, will be vacated July 23. Blue Shield has maintained its quarters on the Midway since 1960, a building with approximately 20,000 square feet of floor space.

The new Blue Shield building in Minneapolis has more than 50,000 square feet of floor space, plus storage area and parking facilities, Paton said.

It was constructed in 1922 as the company headquarters of American Hardware Mutual Insurance Co., and later sold, in 1956, to the Sentry Life Insurance Co. Construction is of reinforced concrete, with exterior walls of St. Cloud granite, Indiana limestone and pressed brick. Architectural style of the building is described as "French Residence."

"In just five years, we've had such substantial progress within our organization that we needed newer and larger quarters," Paton said. "The Midway building served well and readily as our home when we first began rebuilding our service organization for both subscribers and physicians," he added.

Paton said the Blue Shield organization has had three $1 million growth years in the past three years, reaching an all-time record subscriber income in 1964 of $14.5 million. He said that Blue Shield returned nearly 90 percent of this income back to subscribers in the form of payments for their doctor or hospital bills.

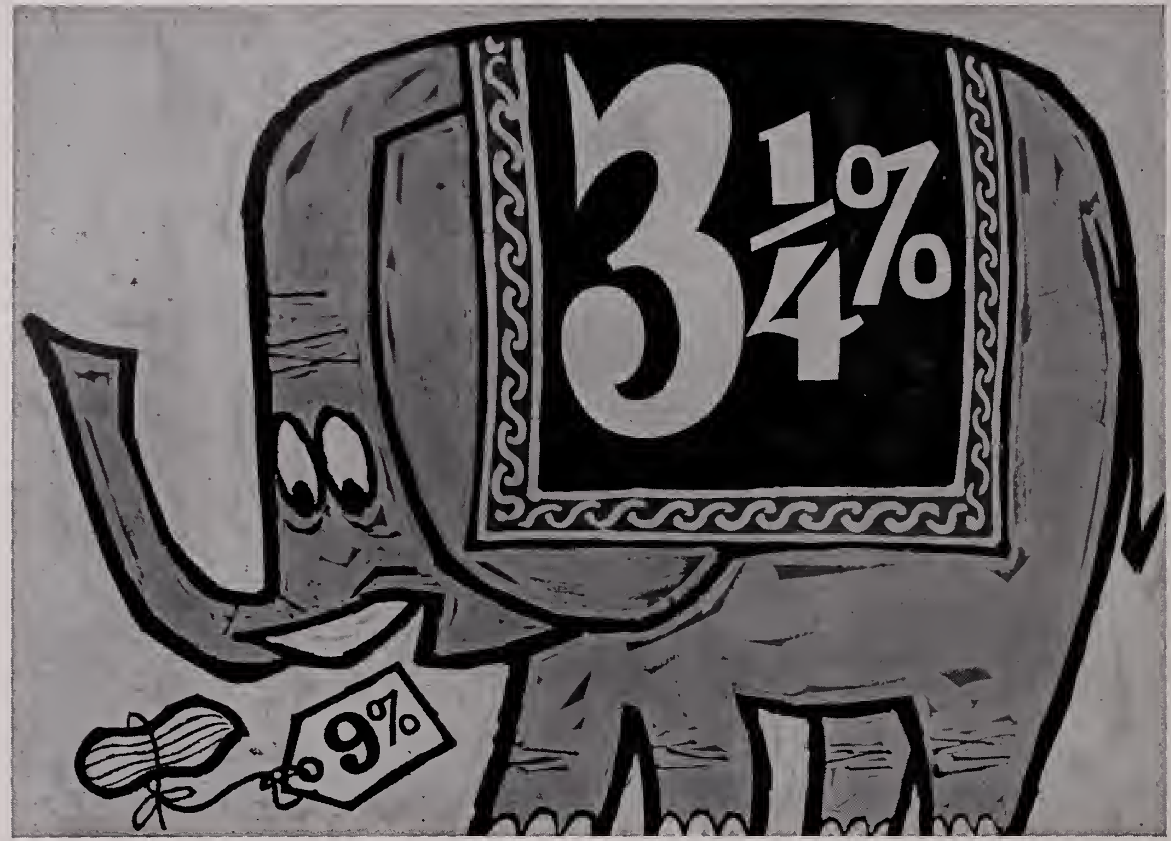
At the same time, he reported, the organization's "reserve fund" — designed to meet future emergencies — has reached the record figure of nearly $4 million. In 1960, the organization had a reserve fund of $3.5 million and had subscriber income of $11.5 million.

For its increased services Blue Shield has added greatly to its personnel roster, Paton said. He said beginning in 1960, Blue Shield had 37 employees, later boosted to around 140 by the end of the year. At the end of 1964, Blue Shield had 194 employees.

The number of physicians participating in Blue Shield has grown since 1960, according to Paton. He said that in 1960 Blue Shield was sponsored by 3,100 doctors of medicine in Minnesota, and today, Blue Shield has gained in medical sponsorship to nearly 3,300 doctors.

By all means go your own way in life. But do it in the same fashion as you go your own way down a crowded street, without stamping on other people's feet or knocking them into the gutter. — The New Age

Riddle: When is 3¼% larger than 9%?



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Over the years, the professional consensus has reflected broad clinical confidence in the marked benefits to be achieved by DONNATAL in a wide range of visceral disorders...in peptic ulcer,[1,6] functional bowel distress,[1] gastrointestinal spasm and discomfort,[2] and other functional disturbances of visceral smooth muscle.

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*This one at Oak Creek, Castle Rock, Arizona

References: 1. Hock, C. W.: Clin. Med. 8:1932, 1961. 2. Marks, L.: Am. J. Gastroenterol. 27:180, 1957. 3. Palmer, W. L., and Kirsner, J. B.: Therapeutics in Internal Medicine, 2nd ed., F. A. Kyser, Ed., Hoeber, New York, 1953, p. 368. 4. Ryan, J. P., Jenkins, H. J. and Robinson, S. M.: J. Pharmaceut. Sciences 53(9):1084, 1964. 5. Vollmer, H.: Arch. Neurol. & Psychiat. 43:1057, 1940. Abst. J.A.M.A. 115:333, 1940. 6. Wharton, G. K., Balfour, D. C., Jr., and Osman, K. I.: Postgrad Med. 21:406, 1957.

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Breast cancer can be highly curable if it is detected early, through regular examinations. Yet, despite all efforts in cancer education and improvements in treatment techniques in the last 30 years,

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While research continues to seek new answers, it is imperative that greater efforts be made to detect breast cancer early and to get women to their doctors when chances of cure are best. That's why the American Cancer Society is encouraging its Divisions across the country to carry out special breast cancer educational programs. Newest of these are demonstration projects in which physicians in a community volunteer one day to giving breast examinations and to teaching hundreds of women breast self-examination. Breast cancer is one of the major cancer problems which we face and which together, doctor, we must try to resolve through intensified research and educational efforts.

AMERICAN CANCER SOCIETY

Annual Meeting Report

Varied Annual Meeting Program Attracted Considerable Physicians Interest

The Minneapolis Auditorium and the Capp Towers provided the setting for the 112th annual meeting of the Minnesota State Medical Association. Rated as one of the most significant meetings in recent years, a number of important actions were taken by the House of Delegates.

The Tuesday, May 18, scientific sessions constituted the Minnesota State Medical Association observance of the 75th anniversary of the founding of the University of Minnesota Medical School. The program included speakers of the medical school faculty and distinguished alumni of world-wide renown.

Minnesota Physicians Receive Numerous Honors

The 1965 meeting was also one at which two distinguished service award winners were announced. Recipients of the award were Drs. O. J. Campbell, Minneapolis, and A. O. Swenson, Duluth.

Winner of the Southern Minnesota Medical Association award for the best scientific exhibit prepared by an individual physician was Dr. Paul J. Bilka. The title of his exhibit was "Examination of Joints; Knee and Shoulders."

Eighteen Minnesota physicians who have practiced medicine for 50 years received 50 Club awards and citations at the annual banquet on May 18.

The following are additional highlights of the 1965 annual meeting.

House Blue Shield Actions Taken

On Sunday afternoon, May 16, the Reference Committee on Medical Economics Reports met in an open meeting to which all delegates were invited to attend. The purpose of the meeting was to consider the report of the Ad Hoc Committee to study Blue Shield. The chairman of the Reference Committee, Dr. Harry B. Hall, presided.

Delegates accepted the complete report, including a series of specific proposals for changes in the governing bodies and policies of Minnesota Blue Shield. The recommendations were adopted without change by the delegates at the closing session on May 18, following an open hearing.

The board of directors of Minnesota Blue Shield, meeting in Minneapolis the following day, took immediate action looking toward conforming to the position taken by the House.

Following is a resume of the House approved recommendations relating to Minnesota Blue Shield:

A. The board of directors

1. The board of directors of Blue Shield shall consist of eleven members chosen from the present geographic areas.

2. The term of each director shall be three-years with a maximum of three terms. This condition applies to elections occurring after 1965. Present members of the board of directors, regardless of past tenure, are eligible for an additional three terms contingent upon the age requirement (see paragraph 3 below).

3. Notwithstanding the provisions of paragraph 2 above, directors shall not hold office beyond that three-year term in which they reach the age of 65. No person who is 65 years of age or over shall be eligible to be elected a director.

4. Present board members over the age of 65 will complete their present three-year term.

5. The corporate body will nominate and elect members of the board of directors. Vote by proxy shall not be permitted.

B. The corporate body

1. New members of the corporate body are to be nominated and elected by the county or regional

Continued

medical society in the same numbers and geographic representation as the House of Delegates. The election of these corporate members shall not be subject to further confirmation.

2. Members of the corporate body shall not hold office beyond the age of 68.

The House does not believe that legislation is necessary to accomplish these recommendations, but if legislation is necessary to accomplish any of these recommendations, they request Blue Shield to initiate such legislation in 1967.

Recommendations with respect to contracts and fees:

A. The House agrees with the Ad Hoc Committee that the concept of usual and customary fees in competitive practice is recognized as the valid determinant of values of medical service.

B. The House agrees with the Ad Hoc Committee in recognizing that a review committee at the local level is essential to protect against abuses and to evaluate the value for unlisted procedures within a plan utilizing usual and customary fees.

C. The House agrees with the Ad Hoc Committee that each county or regional medical society should periodically determine the modal unit value that is being applied to the Minnesota Relative Value Index in its area.

D. Any reduction from usual and customary fee is to be negotiated at the local level as a percentage reduction or discount therefrom. Any percentage reduction will be determined by the individual circumstances of the disadvantaged person or group.

E. Contracts with the Plan A and Plan B fee schedule shall be phased out of existence as they expire. No such new contract shall be issued and no such contract shall be renewed execpt as an indemnity contract after June 30, 1966.

F. All service contracts shall be converted to the concept of usual and customary fees as soon as possible. Recognizing that business considerations may necessitate some delays in such conversion, the House requests Blue Shield to inform the House of Delgates in writing that such conversion will be put into effect as soon as practical. Any reduction from the usual and customary fee is to be negotiated as a percentage reduction or discount therefrom as determined by the individual circumstances of the disadvantaged person or group.

The House of Delegates will look critically upon any unwarranted delay and must be assured that new service contracts with any agency of government be made in observance of the usual and customary fee concept.

The Blue Shield Board is requested to report to the Council in six months and to the House of Delegates in one year with reference to its progress in implementing the above recommendations.

The House of Delegates directs the Speaker of the House to appoint a committee to evaluate the biannual and annual report of Blue Shield, and report back to this House of Delegates. This committee would also be available for consultation with the Blue Shield Board.

Non-Participation Resolution Fails

Delegates endorsed the Reference Committee recommendation that no statement of "Non-Participation" under HR 6675 or similar medicare legislation should be adopted. The action was taken in response to several non-participation resolutions submitted to the Committee. In their stead the House reaffirmed the principles of the code of medical ethics as the basis for medical practice.

The reference committee noted the following compelling considerations concerning the philosophy of non-participation:

1. Hearings concerning HR 6675 are at present being conducted in the Senate Finance Committee of the U. S. Congress.

2. A large number of amendments has already been introduced and, if adopted, may alter the form of legislation should it be enacted.

3. A statement of "non-participation" and flat rejection of the proposed legislation is untimely especially in view of our lack of information as to the final form which the bill may have if it becomes law.

4. A flat statement concerning non-participation will possibly react adversely on opportunities now available to modify favorably the form of any legislation enacted.

The Reference Committee considered that clarification of the doctor-patient relationship could well be presented at this time.

The care of the patient may well involve medical, economic, and religious concepts. The adherence to rigidly dictated terms of treatment might prove detrimental in the personal and medical management of the patient.

The Committee further noted that the Minnesota State Medical Association continues to endorse the concept of allowing the individual physician to employ those acceptable medical techniques and to participate in programs and in patient treatment which are in the best interest of his patient and which are consistent with the doctor's social, religious, and medical training.

The Reference Committee impressed its awareness of the mixed attitudes and emotions held on this resolution but felt the Committee's statement reflected a consensus of opinion.

Usual and Customary Fee Principle Adopted

In another far-reaching action the House adopted unanimously a Council resolution urging Minnesota State Medical Association members to use the usual and customary fee as the basis for all negotiations with any third parties seeking to purchase service medical care for their subscribers, members, or clients.

The resolution observes:

The public has repeatedly sought and continues to seek prepayment mechanisms which cover virtually all medical expenses. The only effective mechanism evolved to date which fulfills this goal and at the same time allows freedom of choice of physicians is the prepayment plan with premium structure geared to payment of the usual and customary fee.

Such plans are presently functioning well elsewhere, both for nonprofit underwriters, such as Blue Shield, and for commercial companies.

There are presently three programs functioning successfully in Minnesota on the usual and customary fee basis, namely, the military dependents Medicare program, the Social Security Disability Determination program, and the Blue Shield "J" Plan sold exclusively on the range.

The sine qua non for success of all usual and customary fee plans has been a conscientious Review Committee at the local level to protect against abuse of the plan.

The only valid determinant of what a given unit of medical service is worth is the usual and customary fee of the physician in competitive practice.

Any reduction from the usual and customary fee will in the future be negotiated on a local level as a percentage reduction or discount. Any percentage reduction will be determined by the individual circumstances of the disadvantaged person or group.

The resolution also states that a medical review committee is to be established immediately in each county medical society to determine annually the modal unit value applied by its members to the Minnesota Relative Value Index. This Committee will also review fees referred to it by any individual or third party requesting such a review.

Copies of this resolution have been sent to all Minnesota State Medical Association members with the June, 1965, Minnesota Newspage.

In accordance with the directives of the resolution, copies have also been sent to the Director of Blue Shield, the Governor's Medical Advisory Committee and the Minnesota Commissioner of Welfare.

Additional Actions Listed

Other matters considered by the House of Delegates included: a resolution from the Renville-Redwood County Medical Society on the DeBakey report opposing the report as a proposal to replace the American system of private medical care with government medicine and directing that the position of the association be sent to the committee of the AMA which is evaluating the report; approval of a proposal from the Public Health Education Committee for a public and physician education campaign emphasizing the importance of protection against tetanus; approval of the recommendation made by the Range County Medical Society for 17 safety features in the manufacture of automobiles as set out in Federal Law PL 88-515 as a measure of controlling death rates on the highways.

Approved a Public Health Education program to emphasize the importance of wearing the AMA Emergency Medical Identification Symbol and the importance of using personal health record cards which provide personal health information including allergies, immunizations, epilepsy, diabetes, and etc.

The delegates rejected a resolution which objected to the confidential section of the birth certificate which gives essential morbidity information as to malformations, Rh

Continued

status and other conditions. In so doing, the delegates went on record in favor of this invaluable means of making available otherwise indispensable information for morbidity and mortality studies.

New Officers Named

Dr. R. P. Buckley, Duluth, was named president-elect at the closing session of the House. Other officers elected were: Dr. Harry B. Hall, Minneapolis, first vice president; Dr. O. L. N. Nelson, Minneapolis, second vice president; Dr. Barnard Hall, St. Paul, secretary (re-elected); Dr. Karl W. Anderson, Minneapolis, treasurer (re-elected); Dr. John T. Pewters, Minneapolis, speaker of the House; Dr. Leon E. Steiner, Albert Lea, vice speaker of the House.

Councilors: Dr. G. R. Diessner, Rochester, First District; Dr. Walter B. Wells, Jackson, Second District (re-elected); Dr. Florian H. Baumgartner, Albany, Seventh District; Dr. John H. Peterson, Duluth, Ninth District. *AMA Delegates:* (3 to be elected) Dr. O. J. Campbell, Minneapolis; Dr. John L. Falls, Red Wing; Dr. A. E. Ritt, St. Paul (re-elected).

AMA Alternates: Dr. J. P. Medelman, St. Paul; Dr. Haddon M. Carryer, Rochester; Dr. Donald McCarthy, Minneapolis; Dr. Walter B. Wells, Jackson. Dr. George Sather, Fosston, is the newly elected chairman of the Council.

University of Minnesota Given AMA-ERF Gift

A check of $16,564.64 was given to the University of Minnesota Medical School at the opening session of the House of Delegates. This is a grant from the AMA-ERF, and it represents the gifts to the University of Minnesota by physicians. It is part of the record $1,313,559.31 contributed in 1964 for medical schools by physicians and their families throughout the country. David A. Pope, a University of Minnesota Medical School freshman from Janesville, Minnesota, was introduced as the 1965 recipient of the Rural Medical Scholarship.

St. Paul was named the host city for the 1966 annual meeting.

AMA President Urges Minnesota Physicians to Continue Medicare Opposition

AMA president, Dr. Donovan F. Ward, was a distinguished guest and speaker at the 112th annual meeting of the Minnesota State Medical Association. A practicing surgeon from Dubuque, Iowa, Dr. Ward is well known to many physicians in the North Central Conference area.

On Monday evening, May 17, Dr. Ward was the speaker at the annual banquet of the Minnesota Academy of General Practice held in the Minneapolis Capp Towers, Hall of Flags.

On Tuesday morning he addressed the House of Delegates at the closing session.

Because of the significance of his remarks, the text of his address to the delegates has been reproduced on the following pages:

"On May 11, the American Medical Association did testify before the Senate Finance Committee on HR-6675; as you well know, the Social Security amendments of 1965. This hybrid bill of overwhelming proportions was passed by the House of Representatives April 8, after a brief debate and without public examination or discussion in the House Ways and Means Committee.

"This proposal, complicated, costly, and containing ominous implications for the nation's economy and health-care system, is the most far-reaching, omnibus bill ever to come before the House in the last 30 years. It would add a compulsory hospitalization plan to the Social Security system, a system which heretofore gave beneficiaries cash dollars instead of benefits. It would authorize a federally-subsidized program of health insurance to cover the medical, surgical, and drug bills. It would expand the present Kerr-

Mills law to cover dependent children, the blind, and disabled persons. It would include self-employed physicians under Social Security. It would increase Social Security cash benefits, give benefits for widows at age 60, amend the disability program liberalize the earned-income limitation into a retirement test, cover cash tips as wages, exempt certain religious sects from Social Security, and do many other things.

"Some of the provisions and objectives of this omnibus bill are good and worthy. Unfortunately, they have been thrown into a conglomerate package which includes a watered-down version of the tired old King-Anderson proposal to provide a limited hospital coverage for everyone over 65, regardless of their need or income; and it would provide it at a cost of a greatly increased tax on the working man and woman. As far as anyone can tell at the present moment, this legislation will cost an approximate 6.6 billion dollars in its first year of operation. To finance the eventual cost, which actually is unpredictable, the bill will raise both the Social Security tax rate and the taxable wage base in a series of increases over the years to come. It will raise the annual Social Security taxes of wage earners and employers from the present maximum of $174 each to $243.60 in 1966, for an increase of $69.60. It will raise the same tax to $369.60 on the employe and $369.60 on his employer by 1987, if we are lucky; and this is more than double the present maximum.

"I quote verbatim from a part of the testimony that the AMA presented before the Senate Finance Committee: 'HR 6675, if enacted into law, will affect the lives of all who live today and the lives of our children and our childrens' children. HR 6675 will introduce into our way of living an entirely new concept of social welfare. HR 6675 will alter the structure of our medical-care system for generations to come.

" 'In the face, then, of so vital a statement, should you not once more pause and consider? You are familiar with the inscriptions on the National Archives Building, which read: 'What is past is prologue,' and study the past to try to gain a glimmering of the shape of things that will tend as a direct result of the action you are being asked to take? Let us examine the past. Let us look for a moment at the government medical systems in other parts of the world. Have national medical schemes resulted in medical help or economic gains? Has the health of the public improved or made gains which surpass those in our country? Has medical science advanced in countries with socialized medical schemes? Have there been economic gains to their people? The answer is no to all these questions. There is nothing in the history of nationalized medical care systems which can lead us to believe, to hope our experience will be unique, and we can hope for no better results here.'

"I also asked the Senate Finance Committee last week: 'Forget for a moment the staggering, though unpredictable, cost of the present program. Ignore the administrative problems that it would create and the burdens it would create for wage earners at the low end of the income scale. Look only at the intrusion of government in the field of medicine, which cannot be avoided if this measure is adopted. With the quality of care thus restricted for the sake of controlling costs, the quality must deteriorate. The patient is the ultimate sufferer. Look again at the experience of foreign programs. The adoption of HR 6675 will set a pattern difficult in the extreme to reverse.' This program cannot be tried out and easily canceled if it proves unsatisfactory. This may be our last chance to ask you to write legislation which will meet the nation's needs, and at the same time avoid the pitfalls of government-financed, government-controlled, and government-oriented health-care systems. This may be your last chance. Weigh the consequences of taking the first step in the establishment of socialized medicine in the United States. While there is still time, we urge you to pause and consider; and here this morning I repeat that plea, and I urge you to repeat it to all the members of the United State Senate. We ask for careful consideration of the Eldercare program, sponsored and supported by the AMA, and favored by an overwhelming majority of the American people.

Continued

"Some may say that it's too late; we should quit; we should not fight against such overwhelming odds. All that I can think of is one of the tunes of the musical, THE UNSINKABLE MOLLY BROWN, 'I Ain't Down Yet.'

"I would like to report to you that I have never seen such cohesion and unity amongst the medical profession. Cohesion is an individual effort; unity is an individual effort. And I must say that the members of the American Medical Association are a cohesive unified body.

"I think I could possibly end this by giving you my idea of how I feel about it by saying a little quote that I sometimes remember from Shakespeare, and it goes thus: 'Lay on, McDuff, and damned be he who cries, Hold, enough.' And I say that we should lay on, and perhaps we might get our way; and perhaps the administrators, the legislators, might say, 'Hold, enough': and that we can win if we will stay in there and pitch."

Remarks of J. M. Stickney, M.D., President of Minnesota State Medical Association, to the House of Delegates — Sunday, May 16, 1965

As the president of your association, it is a challenging and rewarding experience to meet with medical groups and our allied professions in this state and with the medical societies of our neighboring states. Although the president seldom has a major part in making policy, he is constantly asked to explain and interpret the policies which you and the council determine. A review of the president's role in the more than one-hundred years of our existence brings many interesting facts to light. In earlier years he presided at the general convention, and with the formation of the House of Delegates, he became the presiding officer until a revision of the constitution in 1938 established the speaker. Presidential addresses have been delivered before the association in scientific session, at the annual banquet and in recent years before this House. The rather eloquent essays of an earlier time, filled with literary references, have more lately become what might be called remarks appropriate to the day. One is impressed with the fact that many of the problems which earlier presidents considered important enough to discuss are still with us. Always there has been the concern about the best possible medical care for the people of Minnesota, a theme which we hope will never disappear. High ethical and moral standards of intra-professional and public relations were recurrently discussed. The convention of 1869, which entitled itself The First Annual Meeting, adjourned with a request for the members to go home and enumerate the irregular practitioners as compared to the fully qualified and to report on ways of eliminating inferior practice. This intense desire of our predecessors has made Minnesota an outstanding state in the regulation of medical practice. In 1909 Dr. Cornelius Williams made a plea that doctors be paid the same proportion of their charges that the merchants received for their prices from charity patients, and in the 1920's the call to participate in political life lest the medical profession be engulfed by government was repeatedly sounded. We have an adage at the Mayo Clinic that a good solution for many problems faced by a committee may be found by reading the minutes of 10 years ago, and often it is surprisingly true.

Just as we face many problems which have remained unsolved through the years, so do we find that today ours are similar to those of the profession in the neighboring states. I recently had the privilege of visiting the Iowa House of Delegates while they urged "Full and Reasonable Fees" from their Blue Shield organization.

Through the years, crisis after crisis has arisen and the profession has moved forward, often with change, but with integrity and accomplishment. Perhaps the year 1965 represents one of the greatest of the crises. At this moment the details of a new concept in the management of the health care of a whole segment of our population are under discussion before a committee of the Senate. Whether Medicare becomes law or not, we may be sure that a new era is emerging. Hospital administration, voluntary prepayment service or private insurance plans, and probably government are to be our full partners in health care, and with each we must work to produce what only a physician can render, namely good medical care. If, in spite of our efforts to modify Medicare, the law is passed in its present form, we have no choice but to provide the best service we can and to labor to accomplish desirable changes. In our dilemma we must not ignore the other partners aside from government, lest they become our masters rather than our partners. Never before in the years of our cooperation with our medical service associations, Blue Cross and Blue Shield, has it been so necessary that we work with them on friendly intimate terms and they with each other; that we must have our relations with Blue Shield in such order that we can, without reservation, approve it as the Doctor's Plan.

There are many factors in medical practice today which demand that our liaison with the Medical School of the University be close and cordial. There are differences in viewpoints which are inherent in the essential task which the educator and the practitioner face. Each should be understanding of the other's problems, and to this end there is an opportunity for the state medical association to be of service. There is a tendency to place the problem of obtaining physicians to do family practice in the lap of the educator, but I would observe that it is equally the responsibility of the practicing profession to define and create a realistic opportunity for satisfying family practice which will dictate what kind of undergraduate and graduate preparation is essential. The wholesome relationship between educators, specialists and family doctors is an essential ingredient in a healthy state medical association. Agencies sponsored by government and others have suggested a mobilization of resources for research and better patient care which, if implemented, would most certainly involve medical centers and the practitioners throughout the state. Voluntary accomplishment in a sound and progressive program encompassing both research and the practical aspects of medical care will serve to direct future patterns along lines more acceptable to all.

To assure the continued success of the annual meeting it will require persistence and some ingenuity together with cooperation of all sections of the profession. It is the responsibility of this House to determine what type of meeting will meet our needs and how it shall be financed. Better attendance at the scientific sessions and the commercial exhibits is essential if the present format is to continue.

You may wish to give some consideration to making the president's term of office coincide with the year between annual meetings and to the selection of a president-elect for the same period.

It has been a pleasure to serve as your president during the first portion of this term, and I pledge my continued efforts on your behalf in the remaining months. I sincerely thank you and the council for your splendid co-operation and special thanks go to Mr. Brunn, Mrs. Fitzgerald, and the state office staff.

You are invited to send your abstracts to the Abstract Section of Minnesota Medicine, 496 Lowry Medical Arts Building, St. Paul, Minnesota, 55102. Your name and address will be withheld or listed, whichever way you desire.

In Appreciation

The Minnesota State Medical Association would like to express its appreciation to the firms listed below. These firms were technical exhibitors during the recent 112th Annual Meeting of your Association. Their participation in our annual meeting contributed much to its success.

Minnesota State Medical Association

- AAA Leasing, Inc.
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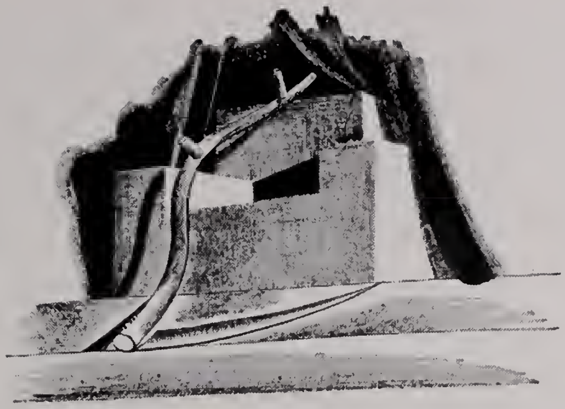

In Memoriam

To be ambitious of true honor and of the real glory and perfection of our nature is the very principle and incentive of virtue; but to be ambitious of titles, places, ceremonial respects, and civil pageantry, is as vain and little as the things are which we court. — Sir P. Sidney

ARTHUR F. BRATRUD, M.D.

Dr. Arthur F. Bratrud, 78, retired Minneapolis surgeon and former president of the Minnesota Conservation Federation, died May 31st. He was born in Fountain, Minnesota and graduated from the University of Minnesota Medical School. Dr. Bratrud practiced medicine with his brother, the late Dr. Theodore Bratrud, in Warren, Minnesota, served in World War I and practiced surgery in Minneapolis from 1920 to 1963.

He was a fellow in the American College of Surgeons and a member of the American Medical Association and Hennepin County Medical Society. Dr. Bratrud was also a 50 Club and life member of the Minnesota State Medical Association.

He is survived by his wife and a daughter.

MARTIN ALBERT NORDLAND, JR., M.D.

Dr. Martin Albert Nordland, Jr., 44, Minneapolis surgeon, collapsed while playing golf on May 30, and died at the golf club shortly thereafter. He was born in Minneapolis and received his medical degree from the University of Minnesota.

Dr. Nordland was a fellow in surgery of the Mayo Graduate School of Medicine from 1945 to 1948 and later left the Clinic to join his father, Dr. Martin Nordland, Sr., in the practice of surgery. He was a member of the surgical staff of the Northwestern Hospital, and a fellow of the American College of Surgeons, member of the American Medical Association, Minnesota State Medical Association, Hennepin County Medical Society, Nu Sigmu Nu professional medical fraternity and the Alumni Association of the Mayo Graduate School of Medicine.

He is survived by his wife and three children.

JALMAR H. SIMONS, M.D.

Dr. Jalmar H. Simons, 80, Minneapolis specialist in gynecology and obstetrics, died June 6th. He was born in Minnesota and received his degree in medicine from the University of Minnesota.

Dr. Simons was a member of the faculty of the University of Minnesota school of medicine for the last sixty years, was on the staff at St. Barnabas Hospital and a department head of Hennepin County General Hospital. He served two terms as president of the Hennepin County Medical Society and was a member of the American Medical Association. He was a 50 Club and associate member of the Minnesota State Medical Association.

He is survived by his three daughters and three sons.

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Physician's Diary

Friendship improves happiness, and abates misery, by doubling our joy, and dividing our grief. — Addison

Dr. Lowell L. Henderson, a consultant in medicine in the Mayo Clinic, was elected president of the American College of Allergists at the annual meeting of the College at Las Vegas, Nevada, April 15th.

* * *

Dr. J. L. Mills was recently honored by Winnebago on occasion of his forty-three years of medical service to that community.

* * *

NEW LOCATIONS: **Dr. J. E. Nord** has opened up an office in Ada . . . **Dr. Arnold M. Berg** of Roseau is moving to Thief River Falls and will practice at the Falls-Starekow Clinic . . . **Dr. L. V. Dahlquist** will be associated with **Dr. F. E. Boyd** at his clinic in Pipestone . . . **Dr. Glen Schroeder** has joined the staff of the Park Region Medical Center in Fergus Falls . . . **Dr. H. W. Henry** of Hinckley has become associated with **Dr. M. S. Munson** at Moose Lake.

* * *

Dr. J. G. Beaton of Northfield recently attended the Fourth Annual Pediatric Post-Gradute Course, Maimonides Hospital of Brooklyn, New York.

* * *

Doctors Keith E. Holley, Allan J. D. Dale, Harry F. Bisel, Frederic C. McDuffie, Panayotis P. Kelalis, Manuel R. Gomez and Ben D. McCallister have been appointed to the staff of the Mayo Clinic as consultants.

* * *

Dr. Robert Gruys of Wells has received the degree of fellow at the 30th Annual Convocation of International College of Surgeons which was held in April in Las Vegas.

Dr. W. D. Brown, Sr. of Minneapolis was recently honored for more than thirty-eight years spent in the practice of medicine. The dinner was sponsored by the Minneapolis Branch of NAACP.

* * *

Dr. Howard P. Polley, head of a section of medicine in the Mayo Clinic and professor of medicine in the Mayo Graduate School of Medicine, was awarded the honorary degree of doctor of science by Ohio Wesleyan University.

* * *

Dr. Howard B. Burchell, consultant in medicine in the Mayo Clinic, has been named editor of Circulation, journal of the American Heart Association. This will become effective January 1, 1966.

* * *

Dr. William H. Remine, head of a section of surgery in the Mayo Clinic, was awarded the honorary degree of doctor of science by the University of Richmond, Richmond, Virginia.

* * *

Michael James Kellum of Minneapolis, a second year student at the University of Minnesota Medical School, has been awarded a $600 scholarship for research and clinical training in allergy by the Allergy Foundation of America. Mr. Kellum will carry out his work under **Dr. Robert A. Good**, American Legion Memorial Heart Research professor of pediatrics and microbiology at the school.

* * *

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WANTED LOCUM TENENS: multi specialty group desires pediatrician for one year. Salary open. Contact — Northwestern Clinic, Crookston, Minnesota.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE — 289; 496 Lowry Medical Arts Building; St. Paul, 55102.

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GENERAL PRACTITIONER WANTED: To associate with six other physicians in a growing and expanding Northern Minnesota Community of 10,000. 130 bed hospital with excellent Pathologist and Radiologist coverage. Early Partnership. Write: P.O. Box 359, Grand Rapids, Minn. 55744.

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— Author unknown

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*Swartz, C., et al.: Circulation 28:1042, 1963.

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1. Goodgold, J., Use of Nicotinic Acid-Glycine Mixture in Treatment of Peripheral Vascular Disease, Clinical Medicine 7:12 (1960).
2. Gustafson, Jr. et al. Use of Glycine in the Treatment of Peripheral Vascular Disease, Surgery 25:539 (1949).

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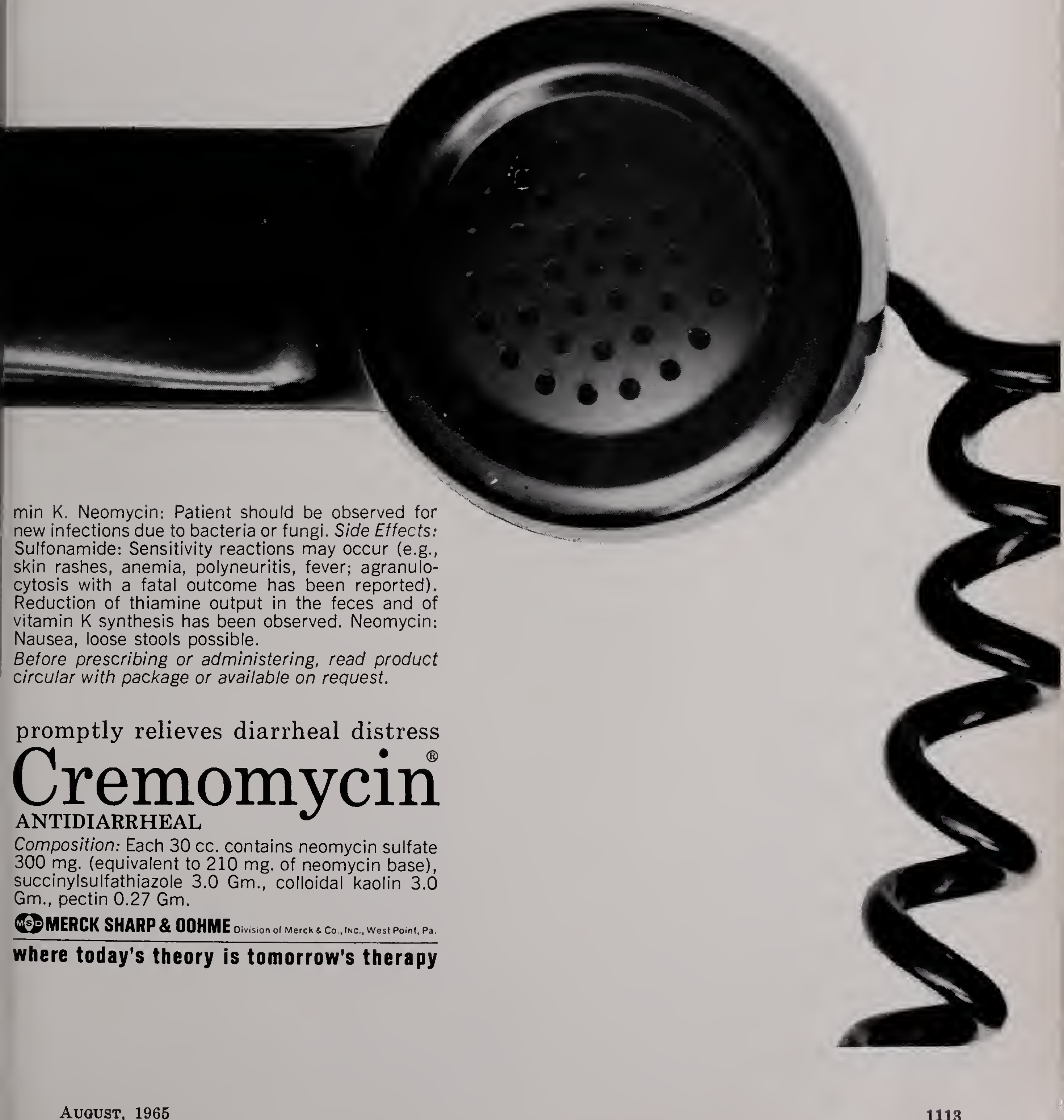

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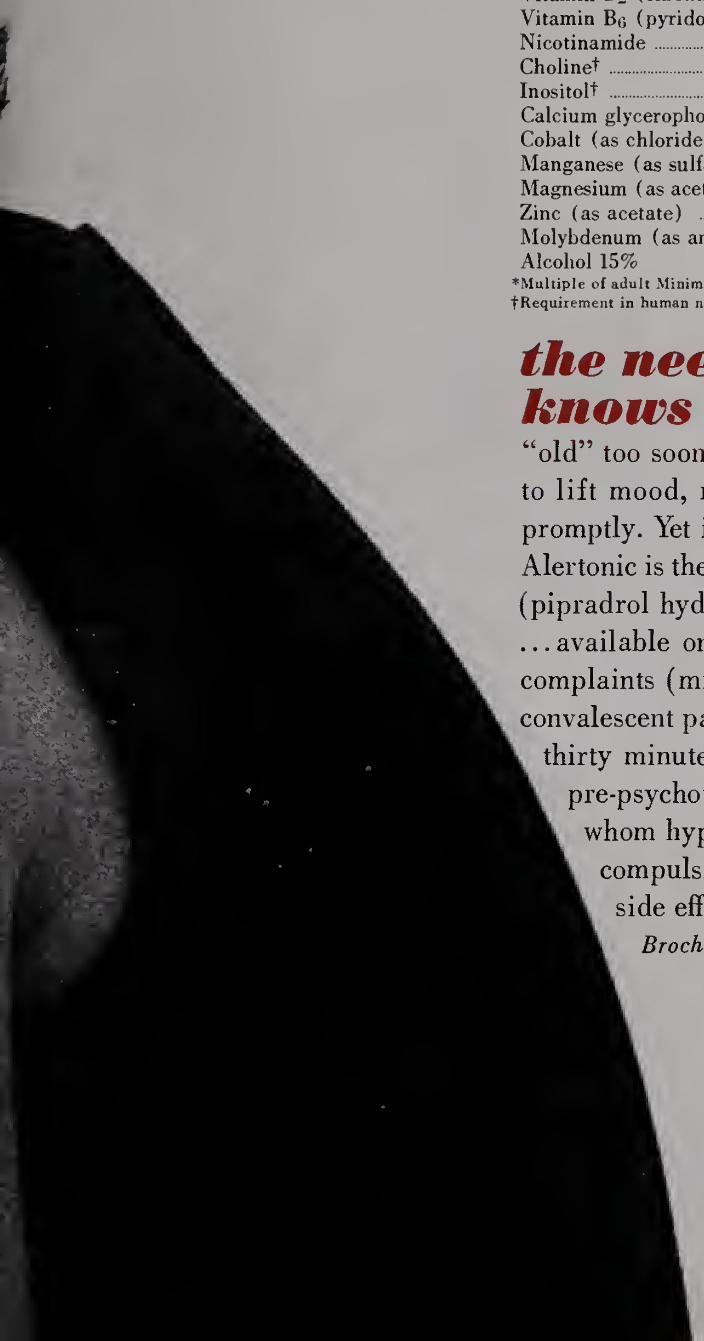

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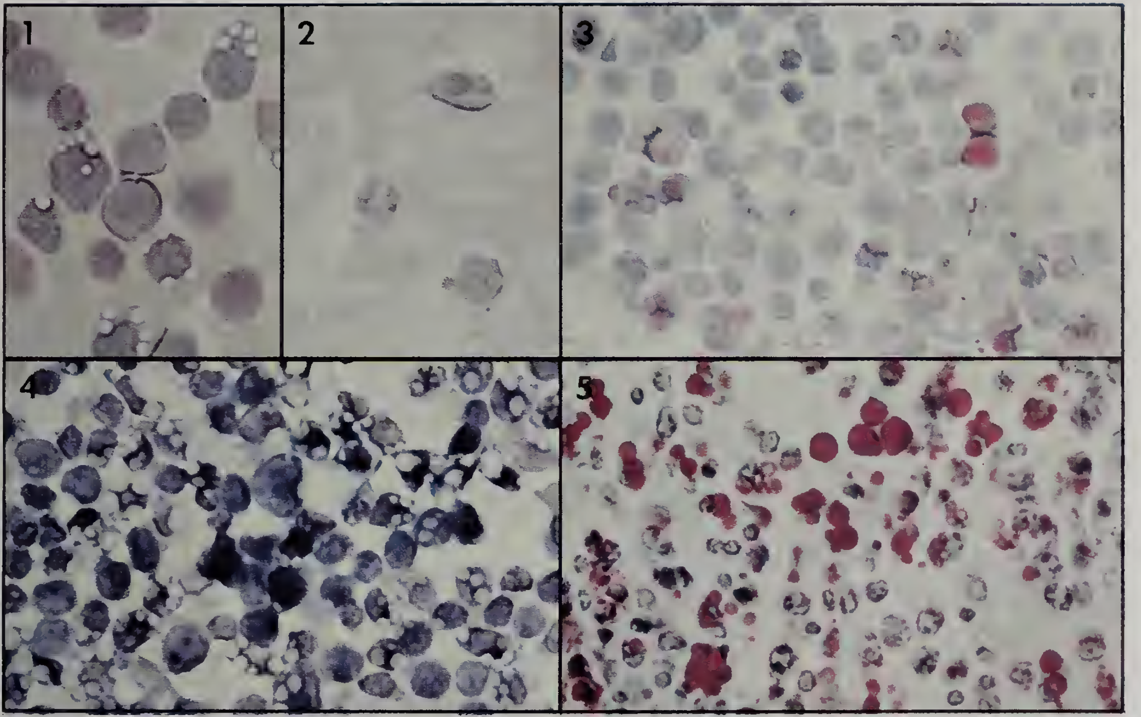

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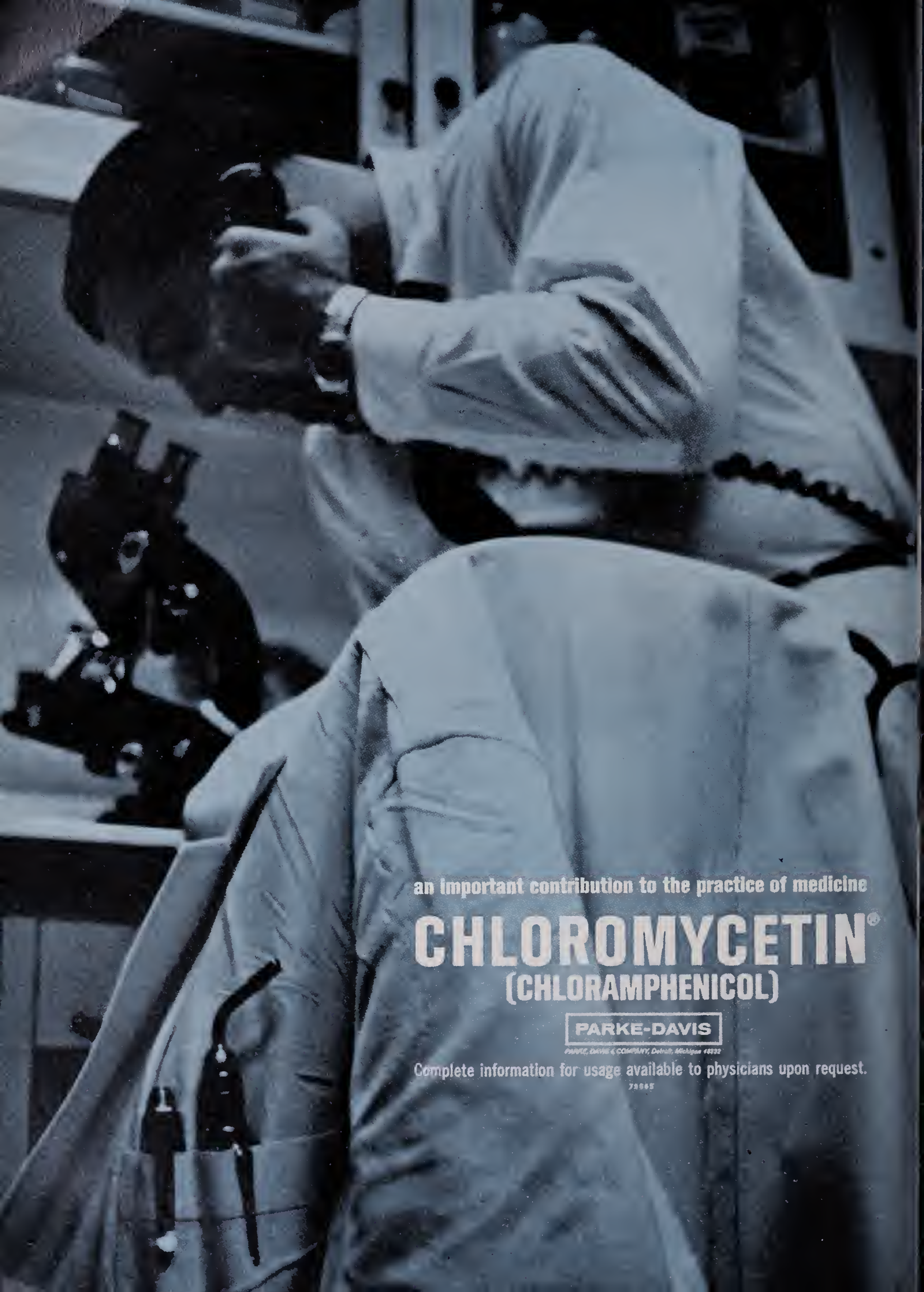

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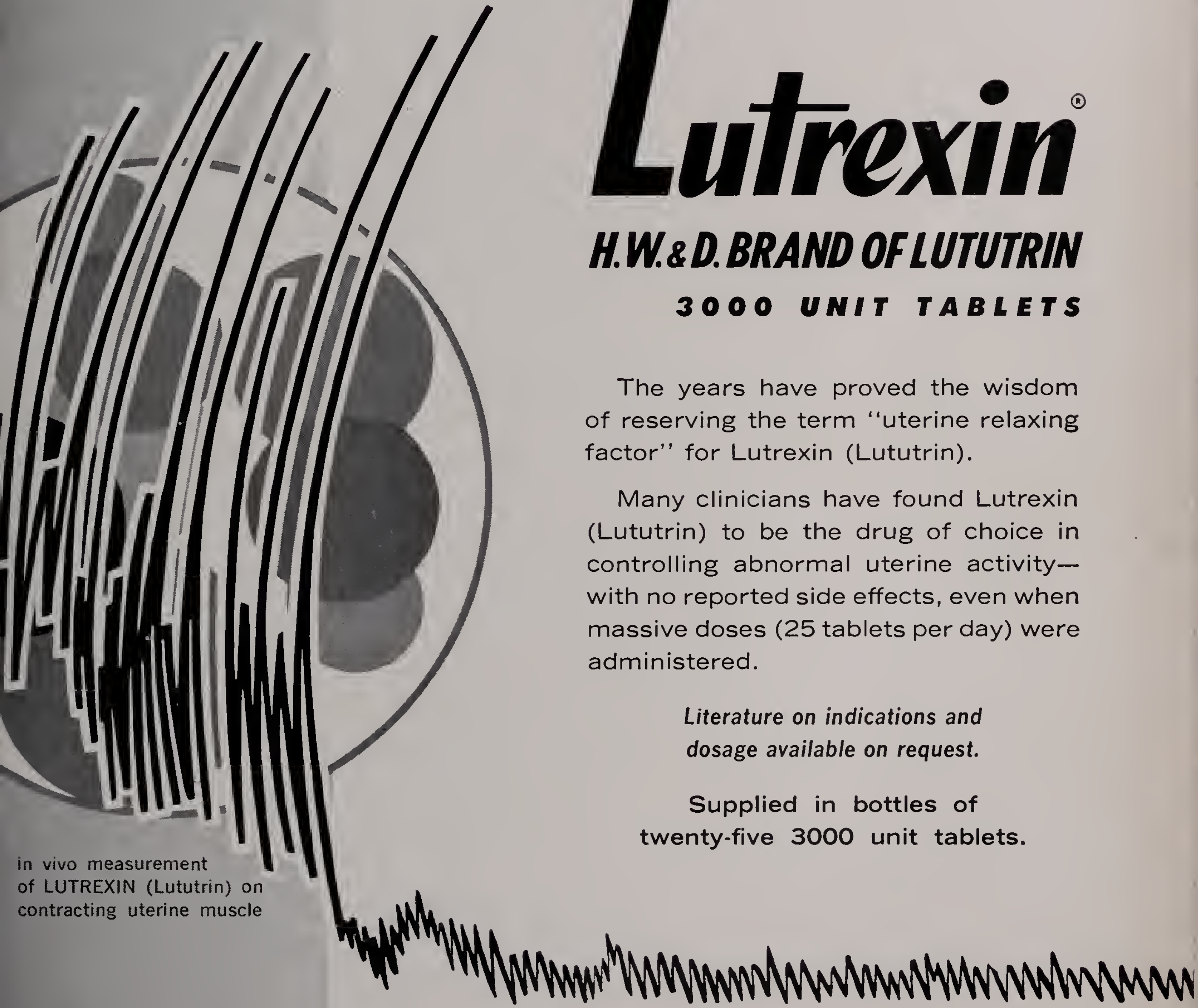

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STATE MEDICAL ASSOCIATION

Volume 48

Number 9

PRESIDENT'S LETTER 1123

ORIGINAL CONTRIBUTIONS

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Hemorrhagic Thrombocythemia as a Cause of Gastrointestinal Hemorrhage
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Mediastinoscopy — A Diagnostic Tool
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Isolated Cervical Tracheoesophageal Fistula
S. Hartley Calin, M.D. and Frank E. Mork, Jr., M.D.
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Reflections of a Neuropsychiatrist in a Court of Justice
Robert P. Jeub, M.D.; Minneapolis, Minnesota 1147

COVER PHOTO:
Giant Russell Bodies in Neoplastic Cells in Leukemic Lymphosarcomatosis. (See page 1125) E. M. Schleicher, Ph.D.

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REF: 1. Boreus & Sandberg, ACTA. PHYSIOL. SCAND., 28:266, 1953.

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President's Letter

The deliberations and actions of the House of Delegates at the 114th Annual Convention of the American Medical Association have become history. There was naturally much professional and lay interest in those matters which pertained to political and economic problems such as non-participation in government programs and the relationship of the AMA to the administrative departments of government. Never before has so much been written about one meeting. Within a few days after its close the official summary by the AMA and the many accounts appearing in the "free" journals and medical newspapers provided up-to-date information. News on this front moves too rapidly to be a fit subject for a letter such as this.

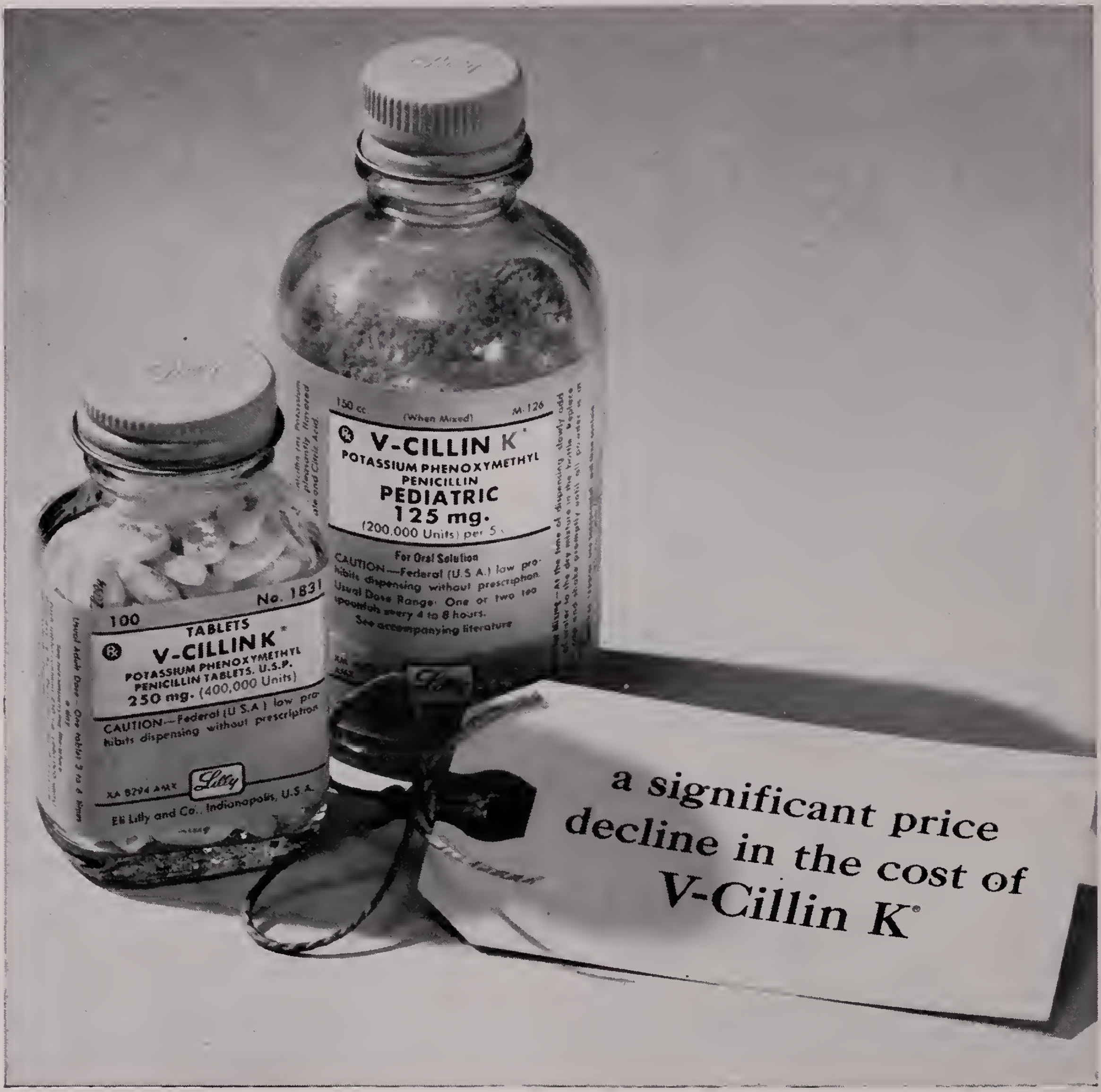
I would like to call your attention, however, to one reference committee report which resulted in postponed action on an important subject to allow time for further consideration. This report dealt with the findings of the Committee to Study the Organization of the House of Delegates headed by past president Gunnar Gundersen. Perhaps my interest was heightened because it was my assignment as a Delegate to chair the reference committee which considered the report of the Gundersen Committee. During the lengthy and sometimes heated discussions it was apparent that we were dealing with an analysis of most of the important functions of a federation such as the AMA. Changes were recommended which would streamline the delegation of authority by the policy-making House of Delegates to its elected Board of Trustees. It was emphasized that the Board must be free to act rapidly enough at all times to be in tune with current issues. To this end, it has been suggested that the Council on Medical Service be responsible to the Board rather than to the House. This council concerns itself with medical-economic problems and has developed what many think is a cumbersome system of subcommittees.

The Gundersen Committee also offers pertinent comment on the relations of the scientific sections of the AMA and the House of Delegates. Each member of the AMA belongs to one of these sections. It was pointed out that the sections are responsible to no unit within the AMA that has jurisdiction over policy. Much attention was also paid to the Council on Medical Education and its proper concern with issues such as the purposes of a medical school, the supply of physicians, and the financing of medical education.

Other items to which the Gundersen Committee gave its attention included the size of the House of Delegates with a suggested limit of 250, the tenure of trustees, and a simplification and clarification of the official policies of the AMA as recorded in the actions of the House and Board of Trustees over many years.

It is my opinion that streamlined organization will not in itself provide a mechanism which will eliminate the stalemates and delays which seem to characterize a professional group as diverse as medicine is, but this thought-provoking report should not be laid on the shelf. Some of the pertinent sug-

Continued on page 1169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Giant Russell Bodies

• in
• Neoplastic Cells
• in a
• Case of
• Leukemic
• Lymphosarcomatosis

EMIL MARO SCHLEICHER, Ph.D.*
Minneapolis, Minnesota

RUSSELL BODIES in neoplastic lymphoid cells have been reported.[1-4] Giant Russell bodies in neoplastic cells in leukemic lymphosarcomatosis, however, seem to be rare. No comparable report was found in the literature.

It is the purpose of this communication to present a case of malignant reticuloma of the lymphosarcoma type in leukemic phase with one to five and more intracytoplasmic giant Russell bodies in neoplastic cells in the primary gastric tumor, lymph nodes, liver, spleen, lungs, small bowel, mesentery, bone marrow, and the peripheral blood as demonstrated by cytochemical methods.

Case Report

A white female, 76 years of age, was admitted to St. Barnabas Hospital on March 9, 1964, with profuse hematemesis, abdominal pain and shock. Blood pressure was 120/70, pulse 94 per minute, respiration 20 per minute, and temperature $100.^2$ degrees. In August 1963 she had had a partial gastric resection at another hospital for a malignant neoplasm interpreted as an "anaplastic carcinoma."

Laboratory Studies and Progress

Hemoglobin 8.5 grams per cent, white blood cell count 5,200, differential leukocyte ratio, stab forms 19, polymorphonuclears 46, lymphocytes 19, monocytes 13, eosinophils 1, basophils 1, plasma cells 1 per cent. Thrombocytes 120,300/c.mm. The morphology of the erythrocytes was suggestive of chronic hypoferremia. Roentgenogram of the chest showed a nodular density in the left lower lobe. Metastatic disease was considered. She received five units of whole blood raising the hemoglobin to 10.3 grams per cent. She was discharged on April 2, 1964.

She was re-admitted on April 9, 1964, in a lethargic and dehydrated state. Her abdomen was distended and various sized areas of ecchymoses were present on the upper extremities and the buttocks. No visible jaundice. No gross loss of blood.

Hemoglobin 7.4 grams per cent, white blood cell count 12,400, differential leukocyte ratio, metamyelocytes 1, stab forms 5, polymorphonuclears 10, lymphocytes 4, monocytes 4, neoplastic lymphoid cells with intracytoplasmic giant globular bodies 76 per cent. Thrombocytes 800/c.mm. Erythroblasts 5/100 leukocytes. Reticulocytes 1.3 per cent. Coombs' test, macroglobulins, cryoglobulins, and cryofibrinogens were negative. Electrophoresis of serum proteins: Total proteins 5.18, albumin 1.53 (decreased), alpha_1 0.59 (increased), alpha_2 0.77, beta 0.94, gamma 1.36 grams per cent. Sternal marrow biopsy showed all marrow units affected by a malignant reticuloma of the lymphosarcoma type. Numerous neoplastic cells with one to many various sized intracytoplasmic PAS positive globular bodies were present. Her temperature ranged between 98 to 103 degrees. She received a total of 1600 ml. of whole blood, raising the hemoglobin to 13.4 grams per cent. She had a progressive downhill course and expired on April 16, 1964.

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*Director Hematology Section, Department of Pathology and Clinical Laboratories, St. Barnabas Hospital.

Autopsy

Gross

The following is an abstract of the autopsy findings. Numerous petechiae were scattered about the entire skin and large ecchymotic areas were on the arms. The pleural cavities contained approximately 100 ml. of clear xanthochromic fluid. The pericardial sac contained 30 ml. of clear fluid. Weight of heart 350 grams. Right lung 600 grams, left lung 450 grams. Soft white tumor nodules were scattered about the lungs and most prominent in the lower lobes. The largest nodule measured 3 cm. The lymph nodes of the hilum showed marked tumor involvement. Weight of the spleen 300 grams. The cut surface revealed dark areas of infarctions. Weight of the liver with the gallbladder attached 1500 grams. Grossly no evidence of tumor. Adrenals and the pancreas were free of tumor. Weight of kidneys 150 grams each. They were free of tumor. Atrophic uterus and ovaries. Generalized adenopathy. The head and neck organs were not examined.

The stomach showed involvement by tumor grossly consistent with malignant lymphoma. A large area of ulceration was present. The small and large bowel showed several various sized tumor masses involving the mucosa and muscle walls. In the mid-portion of the jejunum was a 4 to 5-cm. area containing tumor and in the central portion a large perforation of the bowel 2 cm. in diameter. This segment of bowel was attached to another portion of bowel and mesentery producing a self-sealing process. The mesentery was markedly involved with tumor.

Microscopic

Sections show the presence of malignant reticuloma of the lymphosarcoma type involving the stomach, lungs, liver, spleen, small bowel, lymph nodes, mesentery, bone marrow, and the peripheral blood. Many neoplastic cells contain periodic acid Schiff (PAS) positive globular bodies.

Final Autopsy Diagnosis

1. Malignant reticuloma-lymphosarcoma
2. Perforation of the jejunum due to tumor
3. Bilateral hydrothorax
4. Acute splenic infarction
5. Old subtotal gastrectomy for probable lymphosarcoma

Cytochemical Studies of the Globular Bodies

Air-dried peripheral blood films and marrow smears were stained with Wright's Blood Stain buffered with deionized water pH 5.5. The intracytoplasmic globular bodies were achromatic to this staining procedure. When a diluent pH 6.5 was used the greater number of the globules stained faintly eosinophilic with a more or less distinct bluish rim surrounding the bodies. Figure 1 on the cover of this journal shows the morphology of the intracytoplasmic globular bodies in neoplastic lymphoid cells present in the peripheral blood. When the stain was buffered with a diluent pH 7.2 the bodies showed an affinity to the methylene azure components of the Wright's Blood Stain. The rim surrounding the globules also was more chromatic. Figure 4 on the cover of this journal is a lymph node imprint showing the chromatic character of the bodies and rim.

Hematoxylin-Eosin Staining Reaction of the Globular Bodies

Air-dried peripheral blood films, marrow smears, and imprints of tumor tissue were fixed in formalin vapor for five minutes, washed in deionized water, and stained with hematoxylin-eosin. The globules revealed a strong affinity for eosin.

Unna-Pappenheim Staining Reaction of the Globular Bodies

Another set of formalin vapor fixed smears and imprints were exposed to the Unna-Pappenheim stain for 15 minutes, then rinsed in deionized water and differentiated in acetone. The bodies showed various degrees of affinity for the pyronin dye suggesting the presence of ribonucleic acid in the globules. The rim about the bodies stained faintly reddish-purple.

Periodic Acid Schiff (PAS) Staining Reaction of the Globular Bodies

Air-dried peripheral blood films, marrow smears, and tumor tissue imprints were exposed to formalin vapor for five minutes; rinsed in deionized water; placed in potassium metaperiodate-nitric acid solution for five minutes; rinsed well in several changes of deionized water; exposed to the Schiff reagent for 15 minutes; transferred into dilute sodium metabisulfite solution (10 per cent) 6 ml. to 120 ml. deionized water, three changes two minutes each; rinsed well in deionized water; slightly counterstained with Harris hematoxylin; differentiated in phosphotungstic acid solution (2 per cent); rinsed in deionized water and placed into dilute ammonium water till the preparations turned blue; washed in deionized water and the preparations allowed to air dry. The same staining procedure was applied to marrow and tumor tissue previously fixed in neutral formalin-saline fluid.

Result

The globular bodies showed various degrees of PAS positiveness ranging from very light to deep red. The rim of the globules stained various shades of bluish-red. Figure 2 (peripheral blood), Figure 3 (lymph node imprint), and Figure 5 (section of tumor) on the cover of this journal show the tinctorial reactions of the cytoplasm, globules, and the rim. The different affinities to the PAS reagent of the cytoplasm and the globules may be attributed to a fluctuating concentration of polysaccharides. In general, the cytoplasm is less fuchsinophilic than the bodies, suggesting that the greater amount of PAS positive material is incorporated into the globules. Near the center and upper border of the section of tumor shown in Figure 5 is a neoplastic cell with three giant laminated PAS positive bodies. Whether they are made up of superimposed globules, disclike crystallization of a giant Russell body, or are the result of coalescence of numerous minute globules is not known. The presence of PAS positive globules in histiocytes is noteworthy, suggesting that free bodies are phagocyted. It is conceivable that cells containing bodies that have none or a very weak PAS positiveness may be mistaken for "morular cells of Mott" or "grape cells," although according to Zlotnick[5] these cells are plasmocytes (plasma cells) and generally associated with hypergammaglobulinemia. Since the bodies of the morular and grape cells are invariably PAS negative, erroneous identification of these cells is not likely. It is noteworthy that Russell bodies were present in neoplastic cells undergoing mitosis.

In addition to our cytochemical studies, the staining methods of Pearse,[6] Rappaport and Johnson,[2] and saliva digestion method in conjunction with the PAS reagent were applied to the intracytoplasmic globular bodies. Analysis of our over-all results showed a good correlation with those recorded in the literature. Thus it seemed reasonable to consider the globular bodies in the neoplastic cells in our preparations true Russell bodies, particularly since the bodies were cytochemically identical to the Russell bodies in lymphocytes, plasma cells, and multiple myeloma cells. Whether the rim surrounding the bodies is made up of ribonucleic acid only, as assumed by Pearse, could not be established. That the rim (Russell's delicate cementing substance) is compressed cytoplasmic ribonucleoprotein is more likely.

Russell Bodies and Theories of Origin

Pearse[6] states that "Dr. William Russell in 1890 described intracytoplasmic acidophilic bodies in small round cells at the margin of various malignant growths. He thought them to be fungi and characteristic of organisms of cancer. Russell noted that globule clusters of two to twenty and more were present in the cells, and that the larger aggregates were held together by a 'delicate cementing substance' which stained faintly. For the demonstration of the bodies he used eosin, carbol fuchsin, and iodine green."

Russell Bodies in Plasma Cells

Cells containing Russell bodies were noted by Jordan[7] in the spleen and lymph nodes of the guinea pig and rabbit. According to Jordan the "Russell body cell" arises from the lymphocyte. An intermediate stage of lymphocyte transformation is the plasma cell. He states that the "Russell fuchsin bodies exist in form of spheroidal globules, granules, and crystalloids. They are homogeneous structures with an oxyphilic staining reaction of variable degree, elaborated within the cytoplasm, apparently as the result of some regressive change. Russell body cells apparently represent late stages in a degenerative process." In the Ophthalmic Pathology an Atlas and Textbook, edited by Friedenwald,[8] the following opinion is presented: "A degenerative change of the plasma cell is the plasmacytoid cell. The cytoplasm is no longer homogeneous and basophilic but filled with acidophilic granules. They coalesce and form rosettes around a pyknotic nucleus. These and subsequent forms are known as Russell bodies. The coalescence of the hyaline globular material appears to continue, forming raspberry-like structures, and later large homogeneous masses, usually round (disc-like in microscopic sections) but are occasionally rectangular. They are set free in the tissue."

Pearse[6] is credited with being the first investigator presenting a plausible hypothesis of the development of the Russell bodies in plasma cells. According to Pearse the process is as follows: The faintly Schiff positive plasma cell, generally normal in size, enlarges and becomes increasingly more positive. The material becomes finely granular, associated with a decrease of the staining intensity of the cytoplasm. The granules gradually enlarge and become globular, reaching the size of an erythrocyte or larger. The intensity of staining rises simultaneously. The cell may become so full of globules and the color of the same so deep red that they appear to coalesce. Each body is surrounded by a delicate cementing substance consisting of ribonucleic acid. The bodies failed to bind methylene blue at pH 6. Thus he assumed that the globules were devoid of metachromatic properties. Pearse concluded that "Russell bodies consist of mucoproteins surrounded by ribonucleic acid." He presumed that the mucoproteins are polysaccharides containing globulins (glycoglobulins-mucoglobulins) secreted by the cell.

Hanoaka[9] investigated the origin of Russell bodies in plasma cells employing the supravital technique and the phase contrast microscope. He is of the opinion that the bodies are of mitochondrial origin. Hanoaka advocates that protein synthesis occurs in these constituents of the cytoplasm and that normally the mitochondria are short rod-like or thread-like in shape and under intense irritation enlarge due to acceleration of protein synthesis. The mitochondria become rosary-like and after splitting develop into globules, some progressing to large drops-Russell bodies. Braunsteiner,[10] Braunsteiner and Pakesch[11] observed with the aid of the electron microscope lamellar structures in the cytoplasm of plasma cells. They advance the opinion that the lamellae are protein producing structures. A direct transformation of the lamellae into secretion droplets was observed by these investigators. Lymphoblasts and lymphocytes had no such comparable structures.

Russell Bodies in Lymphocytes

Wislocki et al.[12] found that normal and leukemic lymphocytes contained PAS positive cytoplasmic granules. Rappaport[1] studied patients with acquired hemolytic anemia associated with either chronic lymphocytic leukemia or lymphosarcoma. He noted in neoplastic lymphocytes intracytoplasmic bodies with a strong PAS reaction resembling Russell bodies. Rappaport suggested that the bodies were produced by the cell and that they are comparable with those in plasma cells and multiple myeloma cells. He found neoplastic cells containing PAS positive globules in lymph nodes, spleen, bone marrow, and in reticuloendothelial cells filling the lymph node sinuses. Rappaport saw no plasma cells with PAS positive bodies. Mitus et al.[3] report a greatly increased glycogen content of lymphocytes of lymphatic leukemia and lymphosarcoma. No reference to Russell bodies is made by these investigators. Quaglino and Hayhoe[4] also found a high PAS positive score in lymphosarcoma cells. The positiveness being expressed either in "concentric annular rings of granules or large clumps" in the cytoplasm. The strongest positivity was in patients with widespread disease.

Rappaport and Johnson[2] noted in neoplastic lymphocytes of three cases of malignant lymphoma a single large intracytoplasmic acidophilic inclusion body that had morphologic, tinctorial, and cytochemical properties of Russell bodies. They state that "usually a single globule occupied almost the entire cell body, pushing the nucleus to the periphery. The globules did not have the basophilic peripheral rim, were not as round and as sharply defined as typical Russell bodies of plasma cells." Thus Rappaport and Johnson refer to the globules as "Russell body-like intracytoplasmic acidophilic material." They further observed that the globules lost none of the staining intensity after diastase treatment and that the material was negative for acid mucopolysaccharides. These investigators concluded that "the Russell body-like material is formed by the neoplastic lymphocytes in which it is contained and that the material may represent an abnormal protein (globulin)."

Electron Microscopic Studies of Russell Bodies

Welsh[13] made a comparative study of Russell bodies in plasma cells employing the light and electron microscope. He found that the PAS positive cytoplasmic bodies were in intracisternal spaces and always bounded by a membrane of endoplasmic reticulum.

Isoelectric Point and Size Range of Russell Bodies

Goldberg and Deane[14] found that the isoelectric point of Russell bodies ranged from pH 6.2 to 7.5, reflecting the variation of the isoelectric points of gamma globulins present in the bodies. Thus if the applied stain is on the alkaline side of the isoelectric point of a Russell body the latter stains basophilic (bluish), near the isoelectric point (amphoteric) violet to purple, and when on the acid site the body stains acidophilic (pink to red).

Bangle[15] studied Russell bodies in frozen sections and found them to be colorless. The bodies ranged in size from 0.5 to 30 micra but generally ranged between 2 to 15 micra.

Discussion and Summary

The extensive publications, some of which are cited pertaining to the origin and chemical nature of Russell bodies, correlated with our morphologic-histochemical studies of Russell bodies, suggests a logical sequence of their development.

Normally protein is synthesized by the mitochondria and probably concomitantly a protein-polysaccharide complex is produced. This material is apparently not homogeneous and thus fails to stain or is only faintly PAS positive. At this formative stage the cytoplasm displays a distinct pyroninophilia resulting from the presence of ribonucleoprotein. The PAS positiveness increases with the formation of chondriospheres.* It does not follow that all spheres have a sufficient quantity of polysaccharides to give a positive PAS reaction. As the globules transform into Russell bodies they tend to become more homogeneous. The size and degree of color intensity of the bodies to eosin, pyronin and the PAS reagent seem to be directly proportional to the quantity and quality of ribonucleoprotein, glycoprotein, glycogen, and possibly as yet unknown PAS positive and negative substances present in the individual Russell body. Thus it can be reasoned that when the intracytoplasmic metabolism becomes increasingly uncontrolled morphologic and cytochemical variations of Russell bodies are to be anticipated. On the basis of this supposition it seems justifiable to consider the single large "Russell body-like globule" of Rappaport and Johnson an aberrant form of Russell bodies. This interpretation is supported by the presence of identical globules in our preparations.

It is our opinion that Russell bodies in lymphocytes, plasma cells, and multiple myeloma cells are the result of a greatly accelerated cytoplasmic activity, and giant Russell bodies are the product of a completely disrupted intracytoplasmic metabolic process.

The presence of free Russell bodies in the peripheral blood films, marrow smears, and tumor tissues is likely the result of cell death and or rupture of neoplastic cells by the pressure exerted on the cytoplasm by the bodies. It is noteworthy that histiocytes tend to phagocyte Russell bodies, although their final disposition is unknown. Whether giant Russell bodies are bearers of a malignant stimulus awaits investigation.

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*See Test Your Word Score Page 1167.

Summary

A case of leukemic lymphosarcomatosis with giant Russell bodies in neoplastic cells is presented. No comparable report was found in the literature. The formation of Russell bodies is discussed.

Acknowledgment

Thanks are extended to Dr. Frank B. Johnson, Armed Forces Institute of Pathology, Washington, D. C. for the loan of histologic preparations showing a "Russell body-like globule" in neoplastic lymphocytes; to Dr. Frank E. Martin for allowing this writer to study and report this unusual case; to Drs. N. H. Lufkin, W. A. Chadbourn, and J. G. Popowich, Department of Pathology, St. Barnabas Hospital for their cooperation and support of this research project.

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Magic Numbers

Observance of number is a feature in Pliny's ceremonial; his recipes frequently recommend that the operation be thrice repeated. In the case of curing scrofula by the ashes of vipers he prescribes three fingers thereof taken in drink for thrice seven days. In another application of a Gallic herb with old axle-grease which has not touched iron, not only must the patient spit thrice to the right, but the remedy is more efficacious if three men representing three different nations anoint the right side with it. For a head-wash ten green lizards are boiled in ten sextarii* of oil, and for an application to prevent eyelashes from growing again when they have been pulled out fifteen frogs are impaled on fifteen bulrushes.**

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*About five quarts.

**Thorndike, Lynn: A History of Magic and Experimental Science, Vol. 1, p. 92. The MacMillan Company, New York, 1923.

Hemorrhagic Thrombocythemia as a Cause of Gastrointestinal Hemorrhage

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THE MOST common causes of gastrointestinal hemorrhage are peptic ulceration, esophageal varices, and carcinoma. However, many unusual and rare causes are also described. Hemorrhagic thrombocythemia** has not been included in most considerations of this problem but should be regarded as a diagnostic possibility, though a rare one. This clinical syndrome is a paradox of recurrent bleeding, commonly gastrointestinal, associated with very high platelet counts and frequently with thrombotic phenomena.

Case Report

A fifty-eight-year-old female was seen on December 1, 1962, complaining of three weeks of shortness of breath.

History

The systemic inquiry revealed chronic headaches, chronic constipation without any evidence of red blood or black stools, and usually one episode of nocturia with occasional stress incontinence.

The past medical history revealed a hysterectomy, urinary bladder suspension surgery, anal fissurectomy, and four hospitalizations for acute diverticulitis occurring within the previous nine years. Additional medical diagnoses were chronic anxiety, overweight, myositis of the trapezius and, in 1957, a gastrointestinal hemorrhage with the x-ray findings of a sliding hiatus hernia and a duodenal deformity.

Examination

Examination revealed a weight of 141 pounds and a height of 61 inches. Positive physical findings were pallor, moderate enlargement of submaxillary nodes unchanged for five years, an inconstant grade I and II apical systolic murmur, normal blood pressure, and an obese abdomen.

Laboratory Findings

There were 8.1 grams per cent of hemoglobin with 10,000 W.B.C.s per c.mm. with 62 per cent neutrophiles, 32 per cent lymphocytes, 2 per cent monocytes, 2 per cent eosinophiles, and 2 per cent basophiles with anisocytosis, hypochromasia, and an increased number of platelets in the peripheral blood smear. The initial reticulocyte count was 2.7 per cent; on intramuscular iron therapy it rose to 4.3. The platelet counts were 3.7 million and 3.87 million per c.mm. (Reed and Ecker method with normal values of .2 to .35 million per c.mm.). The blood sugar was 103 milligrams per cent. The serum bilirubin was 0 at one minute and 0.06 milligrams per cent total. There were 6.1 grams per cent total protein with 3.9 grams per cent of albumin and 2.2 grams per cent of globulin. The patient's prothrombin time was 17.2 with a control of 14.1 seconds. The L. E. clot test was negative. The stools were 4 plus with benzidine dihydrochloride testing. The latex test for L. E. cells was negative, as was the urinalysis. The fecal urobilinogen was 40.2 Ehrlich units per 100 grams of feces.

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**See Test Your Word Score Page 1167.

The *bone marrow sections* revealed an increased number of megakaryocytes and platelets. The myeloid-erythroid layer was 2 per cent with the megakaryocytic layer being 12 per cent. There were 0 per cent myeloblasts, 3.8 per cent promyelocytes, 10.2 per cent myelocytes, 15.2 per cent metamyelocytes in the neutrophilic group, 0.4 per cent metamyelocytes in the eosinophilic group, 0 per cent mature eosinophiles, 20.8 per cent mature neutrophiles, 0.8 per cent mature basophiles, 8.2 per cent lymphocytes and 32.6 per cent normoblasts. The developing red cells were normoblastic and there was no evidence of leukemia. The electrophoretic pattern revealed 4.0 grams per cent of albumin, alpha 1 globulin 0.2 grams per cent, alpha 2 globulin 0.7 grams per cent, beta globulin 0.7 grams per cent and gamma globulin 0.5 grams per cent.

The chest X ray and electrocardiogram were normal. The stomach X ray revealed a hiatus hernia and a crater in a deformed bulb.

Treatment and Prognosis

The patient was treated with intramuscular iron, hourly milk and antacids, elevation of the head of the bed, phenobarbital, rest and a progressive Sippy diet. She was discharged in eighteen days with a hemoglobin of 9.7 grams per cent and the stools negative when tested with benzidine dihydrochloride.

Recurrent Symptoms

She was readmitted on February 8, 1963, because of two days of multiple black stools. She had been noticing lower abdominal crampy distress but no upper abdominal distress. She felt a bit warm and moist but had not fainted. The admission hemoglobin was 9.1 grams per cent with a hematocrit of 28 and a platelet count of 2.12 million per c.mm. The same medical regime enumerated above was restarted at this time. The string test suggested upper gastrointestinal bleeding. In grams per cent the blood calcium was 10.3, the phosphorus 4.6 and the uric acid 6.9. Later there were 2.7 million platelets per c.mm. with a prothrombin time of 17.5 seconds with a control of 14.9. Ivy bleeding time was 16 minutes.

By the end of February, 1963, there were 2.6 million platelets with 10.7 grams per cent of hemoglobin and a normal white blood count and differential with many atypical appearing platelets in a peripheral smear. At that time the Lee-White coagulation time was eight minutes, the Ivy bleeding time in excess of 96 minutes, and the Duke bleeding time 40 minutes. The qualitative fibrinogen was normal, with beginning clot retraction at seven seconds and a firm clot with a moderate amount of fluid extruded at 60 minutes. A transfusion of 500 cc. of whole blood was given in an attempt to improve hemostasis, but only one unit of blood was used because of an inability to obtain cross matching due to an anti-Duffy factor.

Additional Observations

The X-ray examination of the esophagus revealed a small sliding hiatus hernia with gastroesophageal reflux, tertiary contractions, and a small pinpoint area with radiating folds suggesting a minimal crater in the hiatus-herniated portion of the stomach. There was also a mild deformity of the superior portion of the duodenal cap, and radiating mucosal folds were visible here as well to suggest ulceration. The X-ray examination of the colon revealed multiple diverticula, especially in the lower descending colon and sigmoid area with irregular margins suggesting some old diverticulitis. A few small diverticula were present in the terminal ileum. She was discharged on a Sippy regime, feeling quite well.

The patient was readmitted on May 2, 1963, complaining again of black stools. At that time the physical examination showed no change except for pallor. Blood studies on admission revealed a hemoglobin of 10.6 grams per cent with a hematocrit of 30; 8,950 W.B.C.s per c.mm., 84 per cent neutrophiles, 11 per cent lymphocytes, 4 per cent monocytes, 1 per cent eosinophiles with one normoblast per 100 W.B.C.s, increased numbers of platelets in the peripheral smear including many atypical forms and basophilic stippling in the red blood cells. There were 1.52 million platelets per c.mm. By May 8, 1963, the platelet count was 1.6 million per c.mm., the prothrombin time was 15.0 seconds with a 14.4-second control. The Lee-White clotting time was nine minutes 30 seconds. The prothrombin consumption test was 54.1 seconds. In one-half hour a clot retraction was complete. She was discharged on a Sippy regime.

Radioactive Phosphorus Treatment

On May 21, 1963, four mc. of P-32 were given orally. Platelet counts came down in two to three weeks as seen in Table 1. Three mc. of P-32 were given on January 7, 1964, and a further drop in platelet counts in four to five weeks was noted.

On May 31, 1964, melena was noted with a decrease in hemoglobin concentration to 12.6 grams per cent with 1.6 million platelets per c.mm., Lee-White coagulation time of 12 minutes, normal prothrombin time, and a prothrombin consumption test of 40 minutes. She was given four mc. of P-32 intravenously and discharged with brown stools testing three plus with benzidine dihydrochloride.

Discussion

There have been two review articles published about this syndrome, which is of unknown etiology.[1,2] The most common symptom has been bleeding, and in the approximately sixty cases reported, as well as in occasional reports since, the gastrointestinal tract has been the common site of blood loss.

TABLE I

Date	Hemoglobin Grams Percent	Platelets Million Per c.mm.	
1 Dec. '62	8.1	3.87	
15 Jan. '63		2.6	
8 February	9.1	2.7	Normal prothrombin time. Ivy bleeding 16 minutes.
25 February		2.6	Lee-White 8 minutes. Ivy bleeding over 96 minutes. Duke bleeding 40 minutes.
2 May	10.6	1.6	Lee-White 9.5 minutes. Prothrombin consumption 54.1 minutes and good clot retraction.
21 May		2.16	Four mc. P-32 orally.
4 June	11.3	.78	
14 June	12.2	1.19	
21 June		1.31	
28 June		1.07	
9 July		1.09	
13 August		1.64	
12 September		1.98	
18 October	12.3	1.42	
20 November	13.0	1.14	Ivy bleeding 12 minutes. Lee-White clotting 20 minutes.
19 December		1.6	
7 Jan. '64			Three mc. P-32 orally.
30 January		1.2	
6 February		1.07	
20 February		.63	
13 March	14.4	.91	
15 March		1.3	
31 May		1.6	Lee-White time 12 minutes. Prothrombin consumption 40 sec.
6 June '64			Four mc. P-32 intravenously.

Laboratory values in patient with hemorrhagic thrombocythemia including treatment three times with P-32.

Peptic ulceration was demonstrated in eight of fifty cases and suspected in several others without confirmation. Ozer et al.[2] reported six cases, all but one of which experienced gastrointestinal bleeding. Only one patient, however, had a history compatible with peptic ulcer. In one instance, recurrent gastrointestinal bleeding recurred over a twenty-seven-year period.

The sex incidence appears to be evenly divided among males and females. The entity occurs most commonly in the middle and older age groups. Less frequent than gastrointestinal bleeding is hemoptysis, hematuria, menorrhagia and excessive bleeding after minor trauma, dental extractions, or operations. Spontaneous bruising often occurs; at times extremely large hematomata are formed after insignificant trauma. Purpura is not seen. Major bleeding occurs after splenectomy; therefore, this surgical procedure should be avoided. Approximately one third develop thromboses which occur in arteries or superficial and deep veins, especially the splenic vein. Priapism has been reported repeatedly.

The platelet counts were increased in all cases and varied according to the methods used. Counts ranged from 0.9 to 14 million per c.mm. with an average of around three million. The platelet morphology was often abnormal with many irregular and distorted shapes, giant forms and chains.

Bone-marrow examination generally has revealed a marked increase in megakaryocytes. The bleeding time has been exceedingly variable. Coagulation time is generally normal, as is the prothrombin consumption test and clot retraction.

Radioactive phosphorus has been found to be effective in treating this disorder in a manner similar to its use in polycythemia vera. As the platelet count falls, the hemorrhages diminish and eventually cease. Judicious repetition of the same or reduced doses of the isotope can maintain a normal platelet level and a good clinical state for long periods. Urethane, X-ray therapy and busulfan[3,4] have also been employed with success.

Summary and Conclusion

Gastrointestinal bleeding occurs commonly in an unusual clinical syndrome called hemorrhagic thrombocythemia, in which hemorrhage is paradoxically associated with an elevated platelet count and frequently with thrombotic phenomena. In this illustrative instance, three episodes of gastrointestinal bleeding were associated with platelet counts up to 3.87 million per c.mm. and an Ivy bleeding time which was in excess of 96 minutes on one occasion. The patient's peripheral blood smear had a marked increase in platelets eight years previously and there was a history of gastrointestinal bleeding five years previously. The primary source of the bleeding could have originated from the questionable crater in a hiatus hernia or from the chronic colonic diverticulitis, though more likely from the deformed duodenal bulb where a crater had been occasionally demonstrated.

P-32 therapy reduced the platelet count. It should be noted that the level of platelet count and bleeding did not always correlate. Also the platelet count and bleeding tendency spontaneously improved in this instance before P-32 therapy.

A platelet count is suggested as a pertinent part of the diagnostic work-up of any patient with gastrointestinal bleeding, as much for the possibility of thrombocytopenia, as well as for the more rare thrombocythemia. Apart from the high platelet count, there does not appear to be any consistent pattern of abnormality in hemostasis or coagulation in this apparently myeloproliferative syndrome of unknown etiology.

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Mediastinoscopy

A Diagnostic Tool*

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THE INCREASING incidence of lung pathology has directed physicians to a number of different diagnostic modalities that can be utilized to determine the exact pathology. These modalities range from simple chest auscultation and percussion to exploratory thoracotomy. Between these, examination of the lung fields can be furthered with chest roentgenogram, bronchoscopy and bronchography, and the scalene node biopsy. This paper is concerned with the diagnostic procedure of mediastinoscopy — a method of examining the anterior mediastinum that is popular in northern Europe.

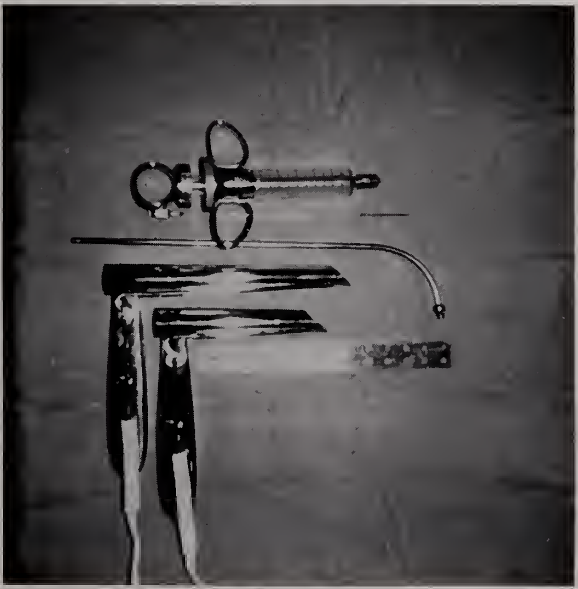

Fig. 1

The function of mediastinoscopy is akin to that of scalene node biopsy in that it attempts to ascertain the diagnosis or extent of pathology without resorting to exploratory thoracotomy. In 1949 Daniels proposed the scalene node biopsy for determining extrathoracic spread of lung malignancy and for establishing the diagnosis in certain nonmalignant cases.[1] The frequency of false negative results has led some to question the efficacy of the scalene node biopsy, especially in lung cancer.[2] In 1954 Harken suggested the use of bilateral cervical mediastinal exploration under local anesthesia with bilateral insertion of the laryngoscope.[3] This procedure is distressing to the patient and unsafe. Radner must be first credited (1955) with recommending biopsy of the paratracheal nodes through a suprasternal incision.[4] However, it was Carlens who put the procedure of mediastinoscopy on a practical basis.[5] One of us was fortunate to be able to work with Carlens in Stockholm.

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Purpose

The procedure of mediastinoscopy has two purposes:

1. To examine the anterior mediastinum and obtain mediastinal biopsies for differential diagnostic purposes when a diagnosis has not been established by more conservative routine methods.

Palva,[6] in discussing the value of mediastinoscopy in the differential diagnosis of anterior mediastinal masses, describes how sarcoidosis can be discerned macroscopically because of the violet-colored, loose proliferating tissue masses found in the mediastinum in the earlier stages. As the condition advances to a more fibrotic form, the glands appear gray and are stony hard. The same stony-hard grayish glands also appear in cases of silicosis of long standing. In addition to obtaining the diagnosis in these diseases, Palva has also utilized mediastinoscopy in diagnosing vascular anomalies, mediastinal cysts and tuberculosis. Koskinen and Linden[7] stress that mediastinoscopy is perhaps most valuable in assessing nonmalignant lesions of the mediastinum.

2. As a means of determining resectability of proven cases of lung cancer by direct palpation, visualization, and biopsy of the anterior and lateral surfaces of the trachea, proximal main bronchi and surrounding structures.

The literature reveals that with present methods, 35-40% of patients subjected to thoracotomy with a diagnosis of lung carcinoma are found to be unresectable at the time of surgery, for even a negative scalene node biopsy does not preclude mediastinal involvement.[8] Reynders, in his institution, raised the resection rate for pulmonary cancer for 60% before mediastinoscopy to 94% after mediastinoscopy.[9]

Technique

General intubation anesthesia is used to prevent coughing during the procedure. A transverse incision is made in the suprasternal area and carried down to the anterior surface of the trachea, just as is done in performing a tracheotomy. This approach avoids danger to the large vessels in the neck, to the thoracic duct, and the apical pleura. It is now important that the very last layer of pretracheal fascia be incised. Once under this layer of fascia, finger dissection is carried out on the anterior surface of the trachea. The innominate artery and the aorta are anterior to the dissecting finger. Overzealous dissection could injure the recurrent laryngeal nerve on the left or the azygous vein on the right. After completion of the finger dissection, the mediastinoscope (Figure 1) is inserted under the pretracheal fascia, and the dissection is extended under direct vision with a velvet eye suction tip. Any suspicious tissue may be biopsied with a small laryngeal or bronchial biopsy forceps, but only after the tissue has been examined for vascularity. This is performed by inserting a long spinal needle through the mediastinoscope into the suspected tissue and aspirating. After biopsy, our experience has shown that any bleeding is minimal and easily controlled with a small gelfoam pledglet. After removal of the mediastinoscope, the subcutaneous tissue and skin are closed in a routine manner. Our series of cases has produced no complications, and this is in keeping with larger series reported from northern Europe.[6,8] Postoperative morbidity is practically nil. The patients are up and about and ready for discharge the morning after surgery.

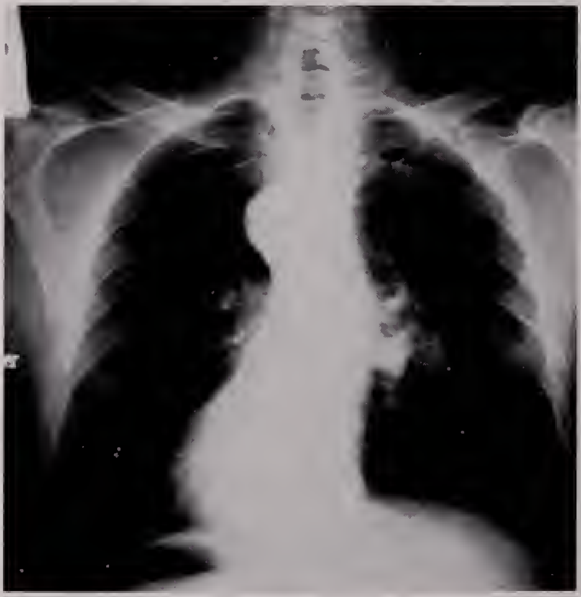

Fig. 2 — *Ed Note: In reverse — excuse.*

Case Report

A 79-year-old white male was admitted to the University Hospitals for the first time on June 8, 1964, for management of a basal cell carcinoma of the nose. Admission chest X ray (Figure 2) revealed an infiltrate in the anterior segment of the right upper lobe. Planigrams of the right hilum suggested a tumor mass. Bronchoscopy on June 15, 1964, was considered normal; however, two sputum examinations revealed cells suggestive of malignancy. In view of this finding, the patient received a course of X-ray therapy to the lung simultaneously with X-ray therapy to the nose lesion. On July 24, 1964, mediastinoscopy was performed under general anesthesia prior to the thoracotomy. Examination of the anterior mediastinum through the Carlens mediastinoscope revealed no abnormalities. The thoracotomy was then performed under the same general anesthesia, and the right upper lobe of the lung resected. The anterior mediastinum was free of any malignant nodes when examined at thoracotomy. The pathologist's report revealed squamous cell carcinoma of the right upper lobe.

Comment

Had the mediastinum been unresectably involved with malignancy, it would have been unfortunate to have subjected the patient to an exploratory thoracotomy.

Conclusions

This is a presentation of a procedure for examination of the anterior mediastinum for diagnosis of unknown masses and determination of extent of pathology. It is safe, with little morbidity. Mediastinoscopy might be beneficial in decreasing the necessity of exploratory thoracotomy in bronchiogenic carcinoma. We are presently evaluating the procedure's ability to eliminate unresectable cases without resorting to thoracotomy. No attempt has been made to tabulate the cases here, although it is planned to do so as the series enlarges. It is our aim in this article to publicize the procedure, technique and purpose so as to disseminate its utilization in this area.

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The Penalty of Overweight

An overloaded stomach is a weight on your brain. — Forbes Epigrams

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Drive Safely

If all the cars on the highway were placed bumper to bumper, it would be Sunday afternoon. — Changing Times

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Derivatively Speaking

Placebo: I shall please: first person singular future tense of Latin *placere,* to please.

Radioactive Isotope

VISUALIZATION OF radioisotopes localized in various parts of the body has become an important aspect of nuclear medicine. Radioisotopes of interest in this regard are those which are selectively taken up by certain organs and/or tissues of interest, and which emit radiations (usually gamma rays) detectable by a Geiger or scintillation counter. The differential isotopic uptake is usually viewed from a recording of the radioactivity as detected by a scintillation crystal as it scans the area of interest.

In most scanning situations, the uptake differential between target and nontarget tissues is relatively low. Thus maximum use must be made of the sensitivity and resolution of detector, analyzer and recorder systems in order to minimize the amount of administered radioactive material and still achieve meaningful information from the scan. The principles of focused collimation,[*] gamma ray spectrometry and photorecording are conventionally used.

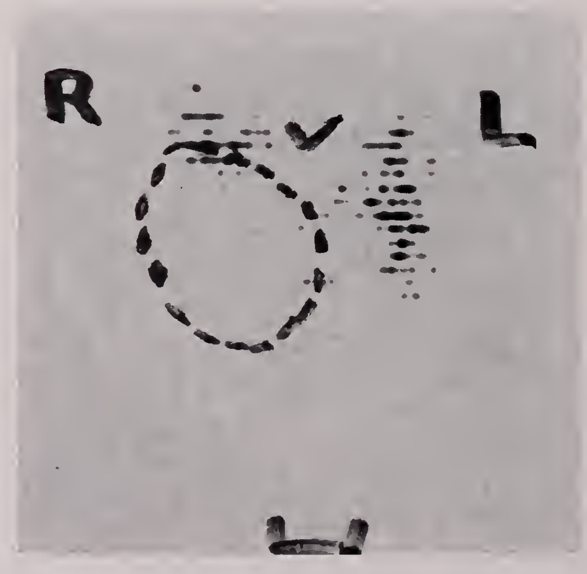

Fig. 1 — Thyroid scan using NaI^{131} showing a cold nodule.

A focused collimator permits a point-to-point relationship to be established between the area being scanned and its recording. The gamma ray spectrometer with its associated circuitry permits selective reception of electrical impulses produced by radiation coming from the target area, while discriminating against those impulses resulting from background radiation. By means of the photorecorder, the electrical impulses passing the spectrometer activate a light that moves in parallel with the detector. This light exposes x-ray film as it moves back and forth. The intensity of the light and consequently the blackening of the x-ray film is directly proportional to the radioactivity beneath the scintillation detector.

Scanning may be done to advantage with the differential uptake by the target tissues being either greater or less than by the surrounding nontarget tissues. Results are generally better when the uptake is greater in

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[*] Presented as an instructional course before the American Roentgen Ray Society, September 1964, and in part before the Minnesota Radiological Society, February 1965.

This work has been supported by grants from the American Cancer Society (Minnesota Division) and Graduate School, University of Minnesota.

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[*] See Test Your Word Score Page 1167.

Scintiscanning*

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the target tissues, since it is easier to detect a small volume of tissue with localized radioactivity than it is to find a volume of similar size that localizes radioactivity less well than surrounding tissues.

Thyroid

Due to a relatively high difference in radioiodine uptake between target and nontarget tissue, the thyroid lends itself particularly well to scanning techniques and was the first organ studied by this procedure.

Radioactive Iodine

Information as to size, shape and location of the thyroid may be gained from scanning following the oral administration of 50 microcuries of I-131 as sodium iodide. The results of thyroid scanning are also quite useful in deciding whether or not a palpable nodule in the thyroid is benign or malignant. Less than 10 per cent of malignant nodules concentrate iodine to any significant degree. A nodule within the thyroid which shows a greater activity in the surrounding tissue is almost certainly benign. A "cold" nodule, on the other hand, has much less diagnostic value because it may be malignant, or even more likely it may be an area of inactive or degenerated thyroid tissue or a thyroid cyst (Figures 1, 2, 3).

Liver

Isotope scanning is helpful in diagnosing liver disease, particularly in situations where the patient is suspected of having metastatic nodules in the liver.

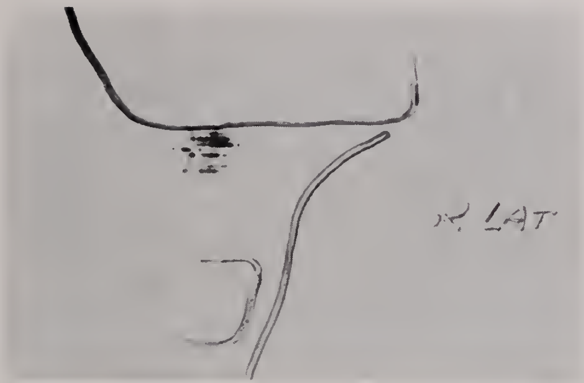


Fig. 2 — Right lateral scan of neck region with NaI^{131} showing sublingual thyroid. (Note lack of activity usual thyroid area).

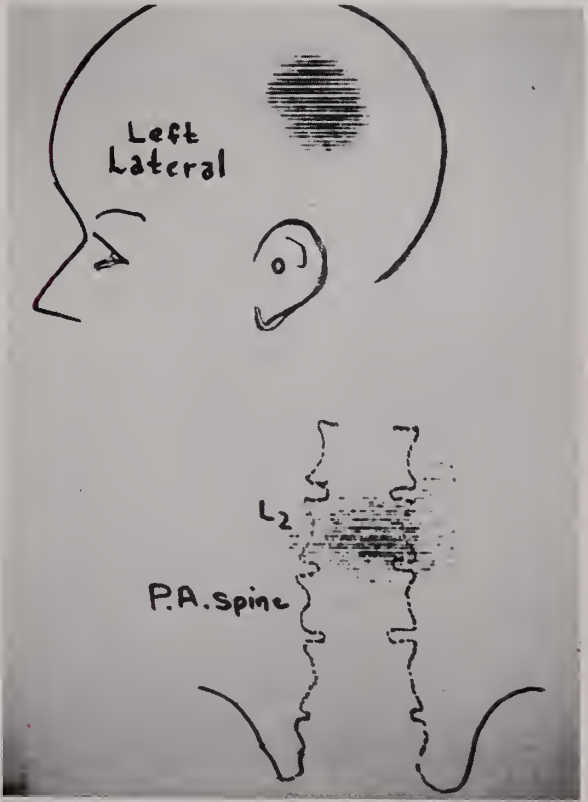


Fig. 3 — Scans with NaI^{131} over areas showing lytic lesions of bone in patient with proven follicular cell carcinoma of the thyroid.

Radioactive Gold

Three materials are being used in our laboratories for liver scanning. These are I-131 rose bengal, I-131 colloidal albumin, and colloidal gold Au-198. The rose bengal is picked up by the parenchymal cells of the liver and subsequently excreted into the duodenum with a clearance half-time of about two hours, although this varies from patient to patient depending upon the functional status of the liver. The colloidal albumin and colloidal gold particles are concentrated in the reticuloendothelial (Kupfer) cells of the liver. The colloidal albumin with a particle size of about 200 millimicrons clears fairly rapidly with a clearance half-time which may vary from one half hour to several hours, depending upon the amount of stable colloid which is administered simultaneously. The addition of 4 mg/kg. body weight of the stable colloid delays the excretion of the I-131 colloid albumin so that a uniform liver image may be produced in the time (approximately one hour) required for this procedure, using a conventional rectilinear scanning system. Colloid gold remains essentially fixed in the liver for the physical half-life of the isotope. Tumors, abscesses and cysts of the liver are not likely to take up any of these scanning materials and may thus be outlined as a negative shadow. Congenital or acquired malposition of the liver and certain abdominal masses may be identified by this scanning technique (Figure 4).

Spleen

Radioactive Sodium Chromate

The spleen may be visualized by a scanning technique using either Cr-51 tagged erythrocytes which have been damaged by heating or I-131 colloidal albumin. Because of the difficulties associated with the treatment of red cells, we have been using the I-131 colloidal albumin exclusively for spleen scans. Colloidal gold is of limited value for spleen scanning, since it is not taken up by the reticuloendothelial cells of the spleen as well as is the colloidal albumin. Recently Hg-203 or Hg-197 labeled Bromomercurihydroxypropane (BMHP) has been made available for spleen scanning. This material binds avidly to red cells, causing moderate damage of these cells so that they are sequestered by the spleen (Figure 5).

Brain

Major effort in scanning at this institution during the past three years has been directed toward the diagnosis of brain tumors. Initially, radioactive iodinated human serum albumin was used for this purpose and concentrated reasonably well in the more vascular brain tumors.

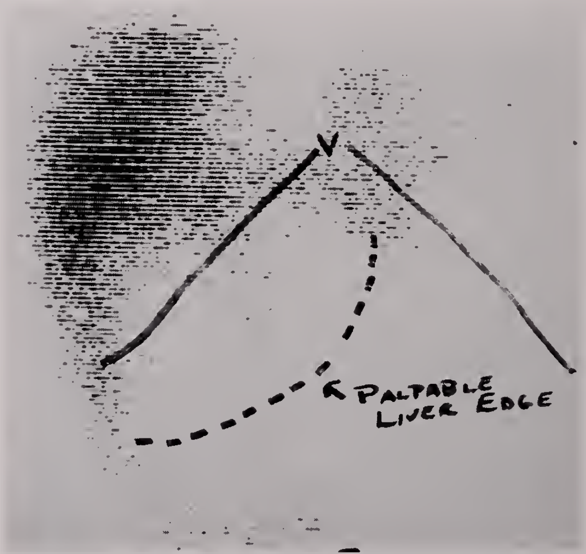


Fig. 4 — Liver scan using colloidal Au^{198} showing large filling defects due to hepatoma. This 18-year-old female also had previous cranial surgery for removal of a glioblastoma.

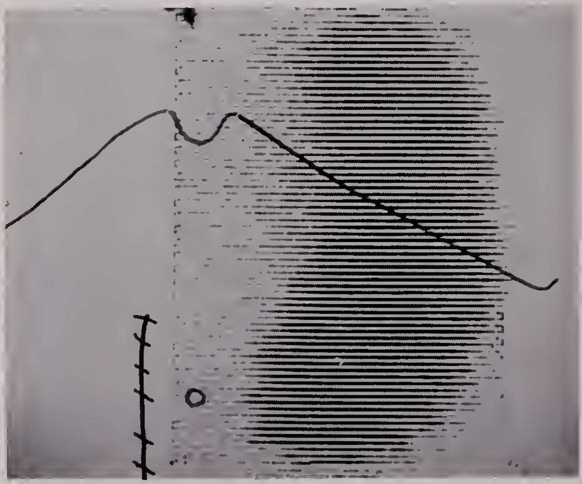


Fig. 5 — Abdominal scan with Hg^{197} mercurohydroxy propane showing marked splenomegaly in a patient with chronic leukemia.

Radioactive Mercury

During the past two years, we have been using Neohydrin tagged with Hg-203 or Hg-197 for brain scans. Our results indicate that scans with either of these agents will delineate brain tumors with about the same degree of accuracy available by angiography and pneumoencephalography We have achieved almost 100% success in detecting glioblastomas. Meningiomas and metastatic tumors have been localized with good success, using two orthogonal scanning planes. Likewise, cerebral abscesses and subdural hematomas have been detected. Relatively avasular tumors such as some astrocytomas are less well delineated. Our over-all success in localizing expanding lesions (both malignant and benign) is better than 85%. Occasionally this scanning method has demonstrated the presence of a brain tumor when other diagnostic techniques have failed and thus is a valuable screening procedure (Figure 6).

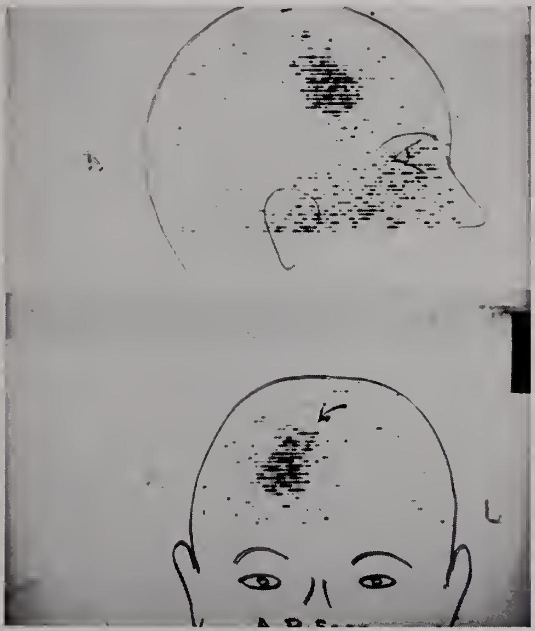


Fig. 6 — Hg^{197} Neohydrin brain scan showing increased activity in a well circumscribed glioblastoma.

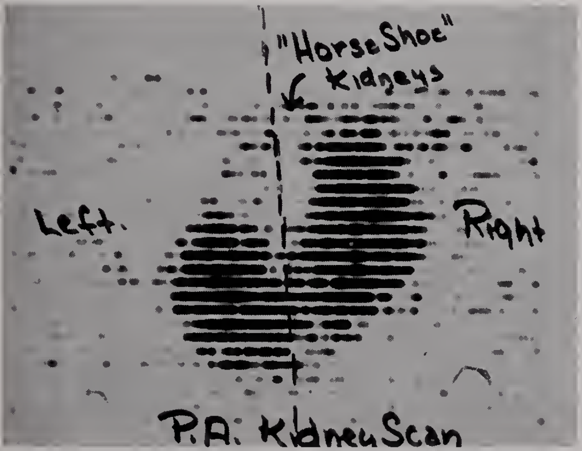


Fig. 7 — Hg^{203} Neohydrin kidney scan of a 3-year-old boy showing a typical horseshoe kidney.

Kidney

Radioactive Mercury-labeled Neohydrin

Scans of the kidneys may be obtained using Hg-197 or Hg-203 labeled Neohydrin. Neohydrin is taken up selectively by functioning kidneys so that kidney scans may be obtained, if desired, with all patients receiving this material for a brain scan. It follows from this that the radiation dose to kidneys constitutes a potential hazard in our technique of brain scanning. Kidney scanning permits exact localization of these organs and allows delineation of filling defects that may be associated with cysts or tumors of the kidney. In addition, a study of the rate and total uptake of Neohydrin by the kidneys yields information concerning renal function. In patients with poor renal function, there may be significant uptake of the Neohydrin by the liver, which may make the visualization of the right kidney particularly difficult because of its anatomic relation to the liver. Hippuric acid tagged with I-131 (Hippuran) has also been used for kidney scans; Hippuran is cleared rapidly from patients with good renal function and is therefore usually infused continuously during the scan (Figure 7).

Pancreas

Radioactive Selenium

We have achieved fair success in visualization of the pancreas, using selenomethionine in which the sulfur atom has been replaced by selenium-75 to provide the necessary gamma emissions. This technique is considered to be a useful adjunct to available diagnostic procedures for study of pancreatic disease. However, certain limitations are encountered which appear to restrict the diagnostic accuracy of the procedure in evaluation of pancreatic neoplasms. There are normal variations in the size and shape of the pancreas and also in the concentration of radioactivity in that organ despite controlled diet regimens instituted to selectively increase the uptake of selenomethione. Thus it is likely that small lesions located near the periphery of the pancreas will be missed. Selenomethionine is also taken up by the liver, which may obscure the pancreatic outline if there is enlargement or down displacement of the liver. Two other factors that should be considered are the relatively high cost of this isotopic preparation and its relatively long effective half-life in the body. The total body radiation dose to the patient receiving 3 microcuries of selenomethionine per kilogram body weight (the usual dose for a pancreas scan) has been estimated to be about 600 millirads. Pancreozynine, secretin, and high protein diet have been used to selectively increase the uptake of selenomethionine by the pancreas. Following the administration of the isotope, glutamic acid hydrochloride is sometimes administered to inhibit the pancreas and thus slow down the release of the radioactivity by this organ (Figure 8).

Bone

Radioactive Strontium

Bone lesions may be demonstrated by radioactive strontium. Two strontium isotopes, Sr-85 and Sr-87 M, have been used for this purpose. Sr-87 M has a rather short half-life of 2.8 hours, so that its application here is very limited. Our efforts have been directed to the use of Sr-85, which has a half-life of 65 days. The metabolism of strontium by bone is similar to that of calcium, although there are some differences in the handling of these elements by the kidneys and gastrointestinal tract. Usually 75 microcuries of Strontium-85 are administered intravenously and the patient is scanned 48 to 72 hours later. This allows up to 50% of the body's strontium content not deposited in bone to be excreted by the kidneys and bowel. It is known that satisfactory scans may be performed in 45 minutes after the injection because of the rapid uptake of this isotope by bone; but the rather high body background at this time makes scanning difficult. Because of the high excretion of Sr-85 by bowel, it is important that laxatives and enemas be used if one is interested in scanning the pelvis or lumbar spine. Sr-85 is taken up most readily by lesions which exhibit osteoblastic activity, although we have found significant uptake of this isotope in lesions which appear on x-

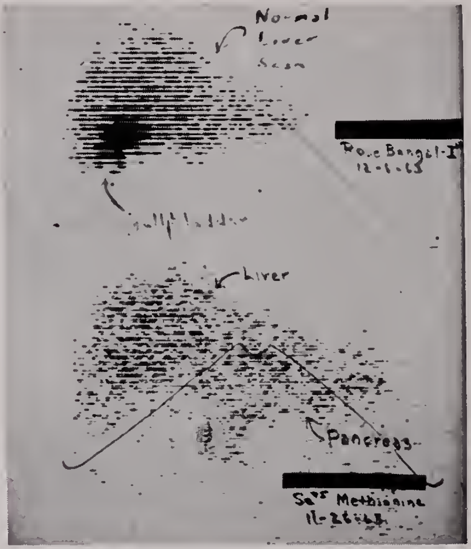


Fig. 8 — Upper scan of liver was performed with I^{131} Rose Bengal and shows filling of the gallbladder. Lower scan was performed subsequently on the same patient using Se^{75} Selenomethionine and shows liver and pancreas.

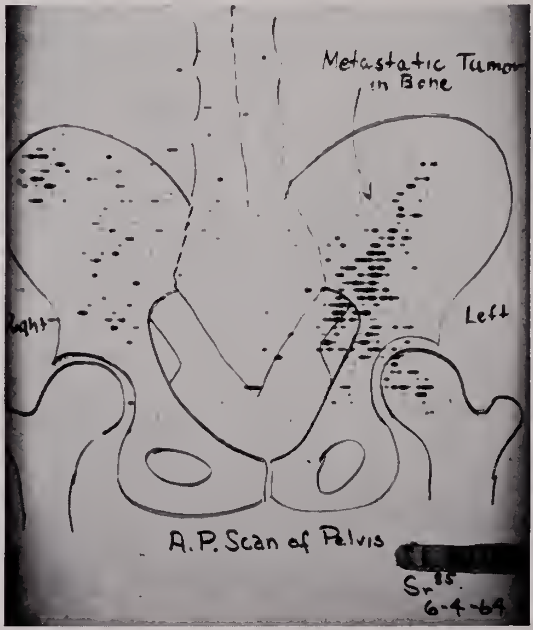


Fig. 9 — Bone scan using Sr^{85} showing lymphomatous involvement in left ilium.

ray films to be primarily osteolytic in character. We are now using this radioisotope for evaluation of patients with possible metastatic disease in bone where there is questionable roentgenographic evidence to support clinical evidence of such metastatic spread (Figure 9).

Lung

Radioactive Colloidal Albumin

Using colloid albumin with a mean particle size of 15 microns and tagged with I-131, we have begun a series of lung scans. This material is administered intravenously and, because of particle size, becomes trapped in the small arterioles and capillaries of the lung. The localization of the material is thus an indication of vascular supply. A dose of 2 microcuries per kilogram is normally administered. This constitutes a dose of 0.1 to 0.3 milligrams of colloid per kilogram of body weight, which then has a clearance half-time from the lungs of about five hours. Experiments with small animals indicate that toxic effects are not encountered below a dose almost 200 times greater than that used for patient studies. Results to date indicate that this procedure may serve as a very simple and useful method for early detection of pulmonary infarcts before any roentgenographic changes are evident. We are also performing the scans on patients with various other forms of pulmonary pathology, including cancer, pneumonia, and atelectasis (Figure 10).

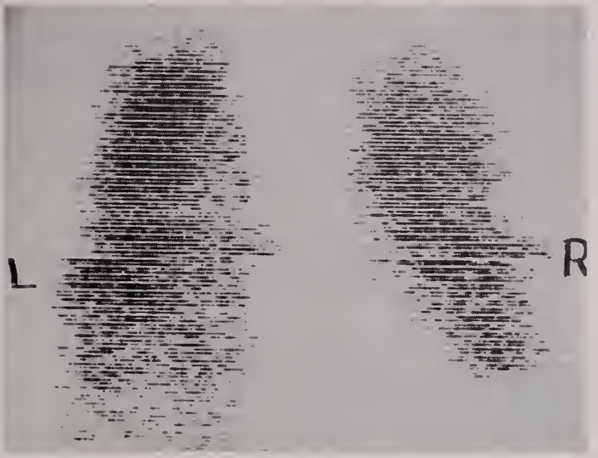


Fig. 10 — Posterior lung scan using macroaggregates of I^{131} albumin showing diminution in perfusion of both lower lobes suggesting pulmonary embolization. Chest x-ray at this time was unremarkable but a repeat radiograph several days later showed evidence of infarction, more marked in right lower lobe. Autopsy one week following lung scan confirmed the embolization and subsequent infarction.

Summary

The future of organ and tissue visualization by radioisotopic means holds much promise. The availability of isotope cameras and very short-lived isotopes will alter, in part, our present approach to isotopic visualization of organs. With these revisions it is possible to complete scans in a much shorter time. It will also be possible to study various dynamic processes such as cardiac, liver and renal function.

CAST SYNDROME

(Hyperextension of the Spine Syndrome)

This syndrome is characterized by dilatation of the stomach, adynamic ileus of the bowel, associated with severe pain in the abdomen and back. There may be persistent vomiting and an electrolyte imbalance may develop.

It usually occurs following the application of a plaster cast to the body.

Treatment consists of inserting a nasal gastric suction tube and a correction of the electrolyte imbalance. In some instances, it is necessary to remove the body cast.

Durham — Encyclopedia of Medical Syndromes. Hoeber

Over-sleeping and over-eating hurt more people than over-working.

— Forbes Epigrams

Isolated Cervical

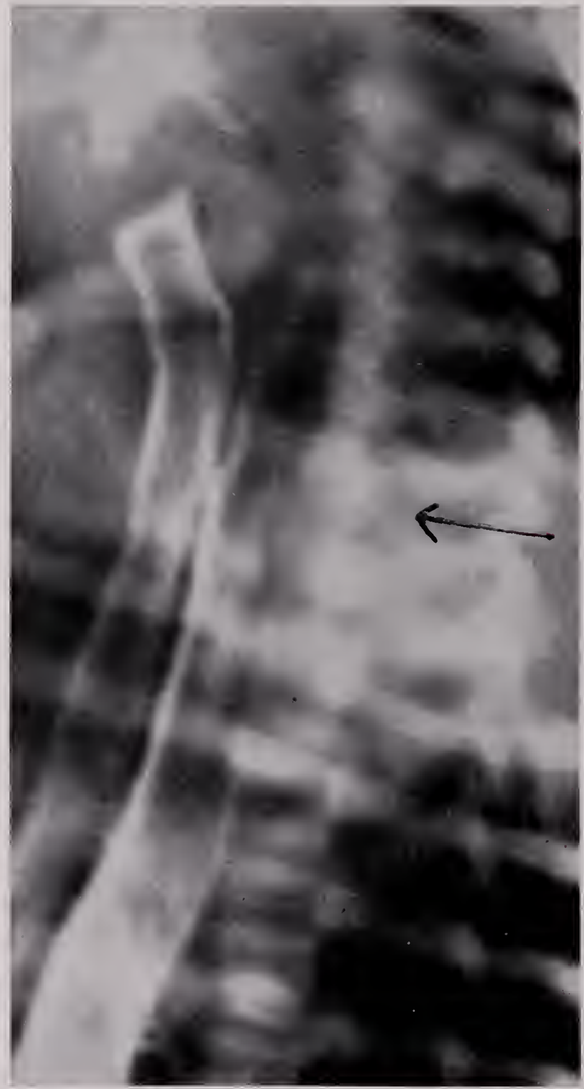
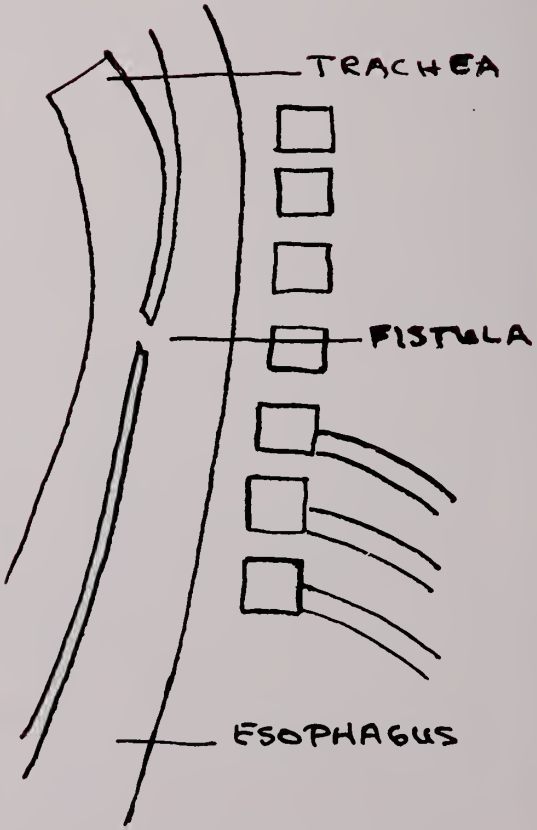


Fig. 1


TRACHEA
FISTULA
ESOPHAGUS

Line drawing of cinefluorograph.

Tracheoesophageal Fistula

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FRANK E. MORK, JR., M.D.*
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THERE ARE two basic types of tracheoesophageal fistula: that associated with esophageal atresia, and the "H-type" fistula without atresia. The former offers no particular problem in roentgen diagnosis; the "H-type" fistula, on the other hand, is especially difficult to demonstrate roentgenographically. Many cases undoubtedly escape the attention of both the clinician and the radiologist. The purpose of this case report is to recommend the use of cineradiography for the detection of this anomaly.

Case Report

A 7 lb., 13 oz. white male infant was born following an uneventful pregnancy. One hour after delivery the infant experienced cyanosis and dyspnea which responded satisfactorily to suction. A chest film revealed no abnormality. The following day the same symptoms recurred during feeding. A nasogastric tube was successfully passed into the stomach, thereby confirming the absence of an esophageal atresia. The infant was subsequently brought to the Radiology Department for an esophagram. Conventional fluoroscopy was performed with the injection of aqueous Dionosil through a small rubber tube in the distal esophagus. The findings were not conclusive, but it was thought that a fistula did exist at the level of the carina. A repeat fluoroscopic examination with multiple spot films was done the following morning, and again the fistulous tract was thought to be present at the level of the carina. A thoracotomy was performed, but the surgeons failed to find any fistulous communication.

About one week following surgery symptoms of dyspnea and cyanosis reappeared after feedings. Upon the insistence of a pediatric resident who steadfastly considered the possibility of an unrecognized "H-type" fistula, the baby was again examined in the Radiology Department. Cinefluorography was performed on this occasion with particular attention directed to the pharynx and proximal esophagus. The film was exposed 30 frames per second. A definite fistulous tract between the esophagus and trachea was convincingly demonstrated at the level of the sixth cervical vertebra, several centimeters below the larynx (See Fig. 1). Interestingly, the fistula was never seen with the child in the resting state, but the communication was repeatedly visualized when the patient coughed or cried. Surgery was again performed, through a small vertical incision on the right side of the neck, and the small fistulous tract was exposed and excised. Postoperative recovery was uneventful. One year later the child was gaining weight and developing normally.

Comment

"H-type" tracheoesophageal fistulas are reportedly quite rare; they are said to account for only 3% of all the congenital tracheoesophageal malformations.[1] A recent review of the literature on the subject showed that over 70 cases have been reported.[2] These isolated tracheoesophageal communications have been found at all levels of the trachea from the second tracheal ring to the carina, with 20% of the reported cases occurring in the cervical area.[3] Of the total 13 cases reported where the fistula was found in the neck, only six have been successfully treated.[3]

Roentgen Diagnosis

The roentgen diagnosis of the "H-type"

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*Department of Radiology, St. Barnabas Hospital.

tracheoesophageal fistula is difficult for a variety of reasons. Many of these problems can be minimized, however, by the routine use of cinefluoroscopy in infants with swallowing problems. First, the fistulous communication can be quite small, often measuring only a few millimeters in diameter. Second, the communication may be in the cervical region where the passage of contrast material may be quite rapid. Third, the fistulous tract may fill only at certain times during the examination. It is better seen when the patient is crying or coughing. Fourth, in the cervical area it can be very difficult to differentiate between aspiration and a fistula, especially in the early stages of life when there is often evidence of inco-ordination in the swallowing mechanism. X-ray examination is best carried out with the child in the lateral or left anterior oblique position. Dionosil is the contrast material of choice. It should be injected carefully through a small rubber tube initially in the lower and mid-esophagus and then in the cervical esophagus. Multiple spot films or preferably cineradiographic films should be obtained of the entire esophagus, with special attention directed to the cervical region if a fistula is not seen in the chest. Finally, in order to prevent the possibility of aspiration pneumonia, care should be taken not to flood the trachea with contrast medium.

Conclusion

A plea is made for the utilization of cinefluorography on any patient who is suspected of having an isolated tracheoesophageal fistula. It is hoped that with the wider use of cinefluorography in infants and children with respiratory or swallowing problems more of these potentially life-threating anomalies will be discovered.

Acknowledgment

Ancker Hospital St. Paul for their permission to use this case for our report.

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2. Schneider, Keith M., and Becker, Jerrold M.: The "H-Type" Tracheo-Esophageal Fistula in Infants and Children. Surgery 51:677, 1962.
3. MacEwan, D. W., Dunbar, J. S., and Murphy, R. R.: Isolated Tracheo-Esophageal Fistula Demonstrated by Cinefluorography. J Canad Ass Radiologists 11:84, 1960.

IT'S THE LAW

An individual is considered to be under the influence of intoxicating liquor when the blood alcohol level is .15 per cent or more.

Arrest is not a prerequisite to the blood alcohol test when the driver has given consent,[1] and an officer is not required to tell the driver of all of his rights under the "blood test" statute.[2] The admission in evidence of a blood alcohol test is not reversible, especially when there is sufficient and overwhelming evidence of the driver's intoxication based on observation a short time after the occurrence of the accident.[3] Written consent is not required for admission of blood test results when the driver has given his oral consent to the test.[4]

The individual who refuses to submit to a blood test for intoxication, insisting that the test must be done by his personal physician can be judged intoxicated on the basis of the arresting officer's opinion[5] and a driver's license can be revoked under the implied consent law if he refuses to submit to a chemical test for intoxication when the arresting officer explains the consequences of his failure to submit to the test.[6]

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1. State of Nebraska v. Seager, 131 NW2d 676 (Neb., Dec. 11, 1964)
2. Gallagher v. Commonwealth of Virginia, 139 SE2d 37 (Va., Nov. 30, 1964)
3. Cesario v. State of Florida, 167 So2d 896 (Fla., Oct. 13, 1964)
4. Dugan v. State of Texas, 377SW2d 201 (Tex., March 25, 1964; rehearing denied, April 22, 1964)
5. Breslin v. Hults, 248 NYS2d 70 (N. Y., March 2, 1964)
6. Chmelka v. Smith, 130 NW2d 423 (S. D., Sept. 25, 1964)

Reflections of a Neuropsychiatrist in a Court of Justice

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MANY OF us have had occasion to appear as expert witnesses before a judicial tribunal and are very much aware of the degree of emotional reaction that directs the participants in a trial. Partisanship on behalf of the defendant or the prosecution plays a continuous role. The law expects medical opinion as to whether or not the defendant is mentally ill and whether or not there is a connection between his mental state and the commission of the act.[1] Constitutional development, coupled with a firmly established conclusion as to the safety of the examination and cross-examination, is dependent upon those participating. The level of performance can scarcely exceed the capabilities of the individuals taking part in the proceedings. Doctors should be able to carefully assess the attitudes of relatives and friends of the plaintiff or defendant. Naturally, by their presence and testimony, a keen observer will know them.

Criminal Responsibility

Criminal responsibility in our state is determined by the McNaughten Rules established one hundred and twenty-two years ago in England. These may be essentially stated as follows: "To establish a defense on the ground of insanity, it must be clearly proved that, at the time of the committing of the act, the accused was laboring under such a defect of reason, from disease of the mind, as not to know the nature and quality of the act he was doing; or, if he did know them that he did not know that he was doing what was wrong."

Some doctors and lawyers feel that this is an inadequate test. Hundreds of articles have been written in support or in criticism of the McNaughten Rules. The District of Columbia in 1954, in the Durham Decision, revived under a different name essentially the same rule as was established in 1887 in New Hampshire by Judge Doe. This test has remained in effect in New Hampshire to the present time and may be stated as follows: "An accused is not criminally responsible if his unlawful act was the product of mental disease or mental defect."

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*Former consultant: Hastings State Hospital; the Youth Conservation Commission; Department of Public Institutions, State of Minnesota.

Attempts have been made to clarify and codify more appropriate rules. In 1960 the American Law Institute issued the following test for insanity: "(1) A person is not responsible for criminal conduct if, at the time of such conduct as a result of mental defect or disease, he lacks substantial capacity either to appreciate the criminality of his conduct or to conform his conduct to the requirements of law. (2) The terms 'mental disease or defect' do not include an abnormality manifested only by repeated criminal or otherwise anti-social conduct."

This rule has not been adopted by any jurisdiction that I know of; therefore, the expert witness must regard himself as a guest in the house of law and behave accordingly, i.e., play the game by the house rules.

There are always differences in the attitudes and opinions of physicians participating in a murder trial. These differences might be resolved if each doctor had at least five years' experience working in a state or federal training school, reformatory, prison, and mental hospital: not in just one of these facilities but in all of them, so that he could understand the longitudinal and cross-sectional history of the accused.

The Accused

There are many disorders that are frequently the subject of expert testimony. These include: (a) sociopath with and without psychosis, (b) paranoid schizophrenia, (c) prison psychosis, (d) emotionally unstable personality with sudden uncontrollable rage, (e) temporal lobe seizure, (f) general paresis, (g) postencephalitis, (h) mental defect with and without psychosis. Since opinion varies and no two cases are exactly alike, the possibility of episodic psychosis or the latent explosion of a confinement reaction or hidden psychosis is certainly overlooked in the transmission to the court of a negative finding such as "not psychotic."

The Sociopath

The most common diagnostic category of individuals who are the subject of criminal law proceedings is the sociopathic personality. The diagnostic criteria are well-documented by Silverman,[2] who found essential similarity with no fundamental difference between the criminal and noncriminal sociopath. These traits vary and may not be as extreme as the following description.

"In the absence of psychotic symptoms or a definite neurosis, noteworthy abnormalities in behavior are the signposts for recognition of the sociopath. A longitudinal review of his life reveals behavior which is reckless, impulsive, unrepressed and often bizarre and pointless. In relation to society he is unproductive, parasitic, and antisocial. In relation to his fellow men he is insincere, untrustworthy, irresponsible, sometimes overbearing and demanding, and often outright hostile. Affect is cold, humorless, and lacking in qualities of genuine warmth, gratitude, and remorse. Close interpersonal relationships are never developed, and the sociopath remains extremely narcissistic and selfish. Sexual relationships are promiscuous, inadequate (deficient) or perverse, and are always lacking in real feeling tone for the object. Efforts are unsustained, interests are fragmentary, and there is lack of any consistent life plan. Although sometimes there is an appearance of brilliance, thinking is superficial and at a plane far below that anticipated from the psychometric test level. If the patient recognizes his difficulties at all, projection thinking is the commonest method of rationalizing them. There is often total disregard for the truth. Insight is usually absent, although one is sometimes confronted with superficial verbal insight. Anxiety is rarely manifest, and then only in response to situational difficulty (e.g., incarceration) which the sociopath has brought on himself. Tolerance to frustration or tedium is poor, and this trait may result in unprofitable, impulsive violent acts, temper tantrums or evanescent psychotic-like behavior. Despite their unsavory and anti-social qualities on cross sectional review, many sociopaths appear superficially intact, pleasant, and likable. It is often only by long contact that the underlying chaotic and sick personality is revealed."

The Lawyer

The personalities of the lawyers also play a role. Those representing the prosecution are merely asking that justice be served and society protected. Those representing the defense bewail the injustices done to the prisoner by uncontrollable forces in society and harass the jury they address with the unfortunate circumstances surrounding the crime. The defense attorney, when unable to predicate facts to the judge and/or jury, strives with the patience of Sisyphus* to indoctrinate his listeners regarding moral aptitudes and social values and their relationship to the defendant. He usually strives to formulate the insanity defense, (viz., that the accused was legally "insane" at the time of the alleged criminal act).

Discrediting the Physician's Testimony

Some lawyers are so wholly convinced of the righteousness of their opinions that they approach the courtroom with schemes to publicly discredit the physician. One might say that physicians who have had little or no court experience should realize that the advocate who harasses and attempts to humiliate a medical witness has already been largely discredited.

Too frequently a physician, about to give medical testimony, has but a one-sided version of the trial issues. Interested patients and their friendly informants might well cooperate by giving only favorable items of information at the unsuspecting doctor's examination.

Others, in their studies, acknowledged the following: "In court the fact that many or all of the participants are unqualified to judge the opinions of an expert witness, or the definitions used by the opposing psychiatrists, leaves all the suggestive powers in the hands of the psychiatrist, regardless of his limitations, who may advise the prosecution — simply because he is the one who has the last word and is inadvertently being directed by his legal counselors, their ingrown jargon and way of thinking."[3]

Explosive Words and Phrases

Further, it has been known for many years that highly explosive words have a serious effect on the jury or the court: words such as communist, atheist, traitor, epileptic, homosexual; and the injection of phrases, such as altered consciences, some impulsiveness, moderately changed, and slight degree, tends to confuse those charged with the operation of justice.

Some colleagues inadvertently use these emotionally supercharged words or phrases to stir up feelings. They consider this technique proper and acceptable for the strategy at hand; however, they cannot always control the effects. The courtroom appears then as a means for the promulgation of suggestion and autosuggestion.

"Well, when human nature falters at times we start planning new laws or procedures. I want to reiterate that the common weaknesses in human nature cannot be overcome simply by the enactment of more laws; is that not obviously so?"[4]

Environmentalists

Furthermore, in recent years we have noted the influence of so-called environmentalists who cry for more and more paternalism. If only we relieve or eliminate this and that type of strain, they argue, we will reduce the incidence of antisocial behavior. Past experience in various parts of the world, where and when emotional stress was most severe, has indicated that neuroticism almost wholly vanished in individuals who had not been freed of their complexes by psychoanalysts! We do admit, however, that parental and group attitudes and behavior greatly influence character development in the adolescent.

As long as we have individuals who are unconsciously but totally dedicated to their own specific cause, and the need to satisfy the revenge and hostility in their own psychobiological structure prevails, they will inadvertently substitute the pomp, ritual, and splendor of the courtroom for common-sense thinking about crime and punishment.

Criminal Proceedings

Criminal proceedings stir emotions. Can

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*See Test Your Word Score Page 1167.

any judicial procedure compare with the emotional impact of certain criminal proceedings? Conflicting testimony is sought; and the laws are plain, particularly those defining insanity as related to criminal proceedings. Intent in advance and competence to understand the ethics of his acts clearly leave other personality characteristics no weight for mitigation. True, there are few to weep for the victim, and those who know the accused wish him no more bad luck than can be avoided in spite of the predicament into which he has gotten himself.

Any judicial proceeding which receives widespread newspaper coverage exerts emotional pressure on those who read the newspapers. Therefore, not only those immediately involved in the trial, but John Q. Public also becomes emotionally involved; because each of us suffers from some repressed feelings or conflicts associated with injustice and inequity in his early years of growth and personality development. This, more than anything else, conditions and corrupts a person's attitudes; and at a conscious level one must clearly realize that, without a deliberate attempt to manipulate, environmental stress becomes an impediment to one's independent thinking.

Other authors[5,6] agree that the expert cannot answer a question directly, but always has to answer the implications of a question in order to avoid the semantic trap frequently used in due process. For example, the physician who replies yes to the following questions: (a) Did the defendant know that he had a knife in his hand?, (b) Did he know that he was stabbing the victim?, (c) Did he know the resistance of that part of the body at the time of the stabbing? — finally must concede that the defendant knew that he was doing wrong. Many forget that the prosecuting attorney has used the verb "to know" in different connotation and not always in the sense of morality: that is, knowing the nature and quality of one's act.

The Witness

The psychological impact of taking the stand for examination and cross-examination places the witness in an inferior position. The strain of cross-examination is well known even to the point of exacerbation of psychosomatic disease, depressive reactions, and also acute coronary artery disease.[7] Under the stress of cross-examination, a person may find himself adhering to opinions he never held. He can be so swayed by his own feeling of guilt (hostility) that, as a witness, he may agree to anything. Some individuals have such a desperate need for approval that they readily give in to a stern cross-examiner. I have several times observed how an intelligent, expert witness, under careful cross-examination, will gradually concede and even contradict his own better decisions and judgment.

Only knowledge and experience can bridge the gap between good intentions and good performance. Using the present judicial system and conforming to the laws in our state, the nondiagnosis of other observers proves to be only a semantic disagreement.

There come to mind instances of murders by adolescent boys. In many, schizophrenia was operative, though in some there was little evidence of this abnormality. Quite understandably the jurors could see only the act of unmodified guilt and dastard criminality. Incidentally, some of these adolescents were adjudged insane by the examining physician at the penal institution following their reception there, and were subsequently transferred to the Minnesota Security Hospital to be detained there until their recovery.

Self-perjury

A physician interrogated in a court necessarily feels exposed. This provokes defensive mental attitudes that become harmful. Aggressiveness frequently causes the witness to say too much. Stuttering, periods of quiet, nervous gestures and the like are frequently interpreted as arising from guilt. One wonders if any person can recognize and understand the subtle subterfuges in a long court session. Many physicians, colleagues, and demagogues alike in neurology and psychiatry, who have served as expert witnesses, have admitted that while under cross-examination they themselves frequently feel on trial and even "almost convicted." The expert never has a chance to explain any multiple-factor theory to a jury. Every official investigative power can easily become a coercive power. Cross-examination, then, is frequently used as a form of emotional exercise doing disservice to factual evidence, and frequently does not get at the truth of the matter per se. This form of self-perjury and consequent self-justification is a well-known passive psychic defense mechanism.[8]

Retribution

Punishment as retribution rarely prevents crime. It may be said with certainty that society, through a group of individuals, takes part in the emotional involvement of a trial. Everyone unconsciously wants to use the paradox of punishment of others in order to relieve tension and conflict in himself. Suggestion, whether conscious or preconscious, perpetuated over the years in due process, social gratification, and prejudice, becomes part and parcel of courtroom procedure. Many people are unable to live out of reach of mental corruption, and their own personal emotional drive seduces them into acting against their moral principles. It is for these reasons that, with recognition of the emotional impact on the seemingly benign courtroom appearance, the expert, through lack of experience and lack of association with due process and the like, can, through no fault of his own, become involved to such a degree that he loses sight of and ignores the goal before him.

A neuropsychiatrist is trained above all in the methods of science. Objectivity is his goal. More so than lawyers, he is expected to free himself from emotional bias; and as his work demonstrates and reflects a closer attainment of this goal, he will better serve the processes of justice when health and welfare are concerned. Engaged as we all are to seek and apply the truth, it is imperative that we should ever be on our guard against the temptations of exaggerated self-interest and also against the actions of a too sectionalized professionalism. The same principles apply, of course, to men in all professions. For it is a fact that mere technical competence does not suffice for the individual, for the profession, or for democracy.

Experience, therefore, allows one to give an unbiased, well thought-out, and clean-cut testimony relevant to factual evidence and criminal intent, and always triumphs over emotional, as well as personal prejudices.

"Experience is the most efficient teacher of all things:" Pliny.

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Overcoming Obstacles

A biologist tells how he watched an ant carrying a piece of straw which seemed a big burden for it. The ant came to a crack in the earth which was too wide for it to cross. It stood for a time, as though pondering the situation, then put the straw across the crack and walked over upon it. What a lesson for us! The burden can become the bridge for progress.

— War Cry

Most of us carry our own stumbling block around with us; we camouflage it with a hat. — Mary Alkus

WHAT'S YOUR DIAGNOSIS?

The patient is a 65-year-old Norwegian farmer who had enjoyed a lifetime of excellent health until three years ago when he began to develop peripherovascular symptoms in his feet and ankles: mainly a cold sensitivity that required long underwear, wool socks, and fur-lined shoes for comfort. Within a year amputation of all his toes was done because of gangrene. One year ago he developed an acute heart failure associated with a hemoglobin of 6 grams. All studies including a bone-marrow examination and GI x-rays were normal. His hemoglobin returned to normal with a "shotgun hematinic" and his heart failure was easily controlled with digitalis.

He was now again hospitalized for study because of increasing pain in his feet and ankles. An oscillometric study markedly decreased total circulation in both legs, but all pedal pulses were full and bounding. An arteriogram showed some irregularities but was within normal limits for his age. X-rays of the legs revealed a generalized osteoporosis. A unilateral sympathectomy was done with no benefit. The pain in his feet and ankles continued to the point where he desired an amputation. Scattered areas of his lower extremities gradually broke down with multiple superficial ulcerations, petechiae, purpura, and superficial thrombophlebitis. The skin color of the legs when in dependent position was usually a mottled, deeply blue color, but on bed rest in the hospital the skin color returned to a more normal, pale, waxy hue. The purpura was usually transitory, but would not blanch on pressure. He was being considered for further amputation in order to obtain relief from pain. The diagnosis was finally substantiated with a laboratory test that could be run in the home with no special equipment.

What is your diagnosis? Turn to page 1177.

Magic Transfer of Disease

In Pliny's medicine there are a number of examples of what may be called magic transfer, in which the aim of the procedure is not to cure the disease outright but to rid the patient of it by transferring it from him to some other animal or object. Intestinal disease may be transferred to puppies who have not yet opened their eyes by pressing them to the body and giving them milk from the patient's mouth. They will die of the disease, when its cause and exact nature may be determined by dissecting them. Griping pains in the bowels will also pass to a duck that is held against the abdomen. One may be rid of a cough by spitting in a frog's mouth or cure catarrh by kissing a mule, although in these cases we are left uninformed whether the disease passes to the animal. But if a person who has been stung by a scorpion whispers the news in the ear of an ass, the ill will be transferred to the ass.*

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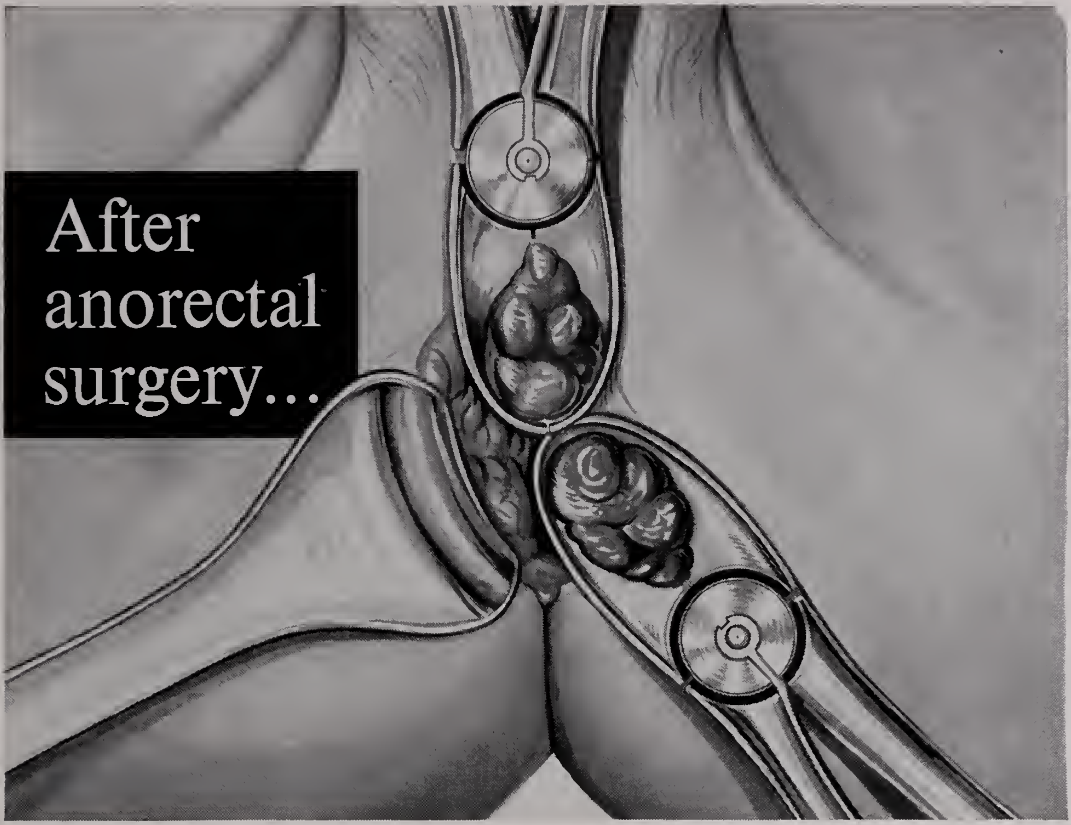
*Thorndike, Lynn: A History of Magic and Experimental Science, Vol. 1, p. 88. The MacMillan Company, New York, 1923.

Nature gets more dependent on man with each generation. My father rose high with little more than muscle and courage. But in my time I had to add germ killers, and now my kids need vitamins, psychiatry, and miracle drugs.

— Better Homes and Gardens

If fate throws a knife at you, there are two ways of catching it — by the blade and by the handle. — Oriental proverb



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Editorials

Views of a Trial Judge on the Medical Witness with Emphasis on the Neuropsychiatrist and the Mentally Ill

I WRITE HERE today as a friend and not a critic of both the medical and the legal professions. All of us, be we doctor or lawyer, take pride in the fact that we are professional men. It is basic that the doctor and lawyer have much in common and are fellow professionals working toward common goals.

Unfortunately, one of our main areas of difficulty, and sometimes downright hostility, has to do with the reaction of the medical witness to his stint in the court room. Medical witnesses have many criticisms of the legal procedure, and some of them are well taken. There must be a realization on the part of the medical witness that the legal system is an adversary system. Naturally, the adversary system is quite foreign to the man of medicine. He is educated and trained and practices under an entirely different tradition. Doctors have to realize that it is the adversary system that leads to the discovery of truth and, further, they will have to learn to live with it because it is here to stay.

On the other hand, of course, it is incumbent upon those of us who operate within the legal system to do our very best to make the system more workable and less, shall we say, "adversary." I do believe that the most serious and sound complaint doctors have is that they are not permitted to rely, in stating their opinion, on reports they have from other experts and in some cases not allowed to rely on the office history. This complaint is well taken. Which doctor, in forming the diagnosis of a patient who has come to him, does not base it, in part, on laboratory reports, findings of a radiologist, or reports from other specialists? Similarly, doctors take the patient's history as a matter of course, and find it an important guide to diagnosis. If the standards of the hospital and medical school are to be brought into the court room, then doctors should be permitted the same freedom on the witness stand to express an opinion based on any information that they consider reliable. Fortunately, the law of evidence is clearly moving in that direction.

The area that is most controversial at the present time in the medical and legal professions is the field of neuropsychiatry and its relationship to crime and the defense of insanity. Our courts have been operating under the M'Naghten Rules for over a hundred years, which basically require that "to establish a defense on the ground of insanity, it must be clearly proved that the accused did not know the nature and quality of the act he was doing or, if he did know it, that he did not know what he was doing was wrong." Many psychiatrists and jurists feel

Continued

"All Registered Nurses are Alike"

It stands to reason. They all go through the same training; they all have to pass the same tests: they all have to measure up to the same standards. Therefore, all registered nurses are alike.

That's nonsense, of course. But it's no more nonsensical than what some people say about aspirin. Namely: since all aspirin is at least supposed to come up to certain required standards, then all aspirin tablets must be alike.

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You might also say that all registered nurses aren't alike, either.

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that this is a bad test at best. However, as yet no scholars have managed to come up with a satisfactory alternative and until that happens, I will, reluctantly, have to be one of those who would resist change.

M'Naghten is denounced as unjust to the defendant. It is called arbitrary in the light of modern psychiatric knowledge, and I agree that it is, but the proposal to replace it with another definition of legal insanity contains two flaws. One is the naked assumption that insanity should bear on the determination of guilt as opposed to the post-conviction disposition of the offender. The other is that the very thesis of the attack upon M'Naghten demonstrates that the proposed substitutes are equally arbitrary and incompatible with the psychiatric view of man. However, it is the court's feeling that the real problem that the neuropsychiatrist is having in criminal cases is due not to the formula laid down by the court but because the psychiatrist has attempted to usurp the role of the judge and jury in cases wherein insanity is pleaded as a defense.

Unfortunately, the psychiatrist of today in many instances has attempted to become the expert in sociology, anthropology, philosophy and law. He has attempted to answer questions of legal significance pertaining to mental status — legal, moral, ethical, philosophical questions — instead of straight psychiatric problems. Man has been debating these issues for centuries and has not resolved the difficulties. An entire system of law has been devised to deal with these polemics as they affect social transgressions. However, this resolution belongs in the province of the judge and jury. While it is true that psychiatrists have a special knowledge as to medicine and mental illness, when it comes to the recognition of responsibility, which is a moral and legal problem, their knowledge is no greater than that of the minister, philosopher or judge.

Dr. Robert Jeub in his excellent article in this issue,* entitled "Reflections of a Neuropsychiatrist in a Court of Justice," falls into this error. It is apparent from his reaction to court work that he fails to realize that the majority of neuropsychiatric problems arise from the witness extending himself into fields in which he has no business. His reference to the fact that prosecutors are merely seeking justice and defense attorneys something less constitutes naivete at its worst. Perhaps it would be much better if experts in all fields, including neuropsychiatry, learned the use of the words, "I don't know," when the examiner tries to lead them outside their special field of knowledge.

In fairness, it must be admitted that the experts in the psychiatric field have been driven to some extent by the public and by the courts and the lawyers in expending their area of *expertise*, because lawyers and courts have wrongly continued to ask their help in problems outside their special field. Actually, this trend has been unfair to the psychiatrist, who may be of great help to the courts if his testimony is confined to medical-psychiatric issues rather than to the greater issues of morality and legality.

It is the awesome responsibility of the law to determine when a man is responsible for his behavior, and it is the duty and the responsibility of the psychiatrist to help the law make that determination by sharing with the law only his knowledge of mental illness and its relation to behavior. If psychiatrists were held to their special medical knowledge in the court room rather than attempting to extend it to areas not within their special domain, they would escape with less drastic results to the sanctity of their offices.

Therefore, it is imperative that the psychiatrist, the lawyer and the court work together to leave the moral questions involved and the opinions of responsibility to the court, with the aid and assistance of good forensic psychiatry confined to its speciality of medical knowledge.

The truth is that insanity should have nothing to do with the adjudication of guilt but rather should bear only upon the disposition of the offender after the conviction and, therefore, the contest concerning M'Naghten and its competitors is a struggle over an irrelevancy.

Lawyers, by improving their treatment of

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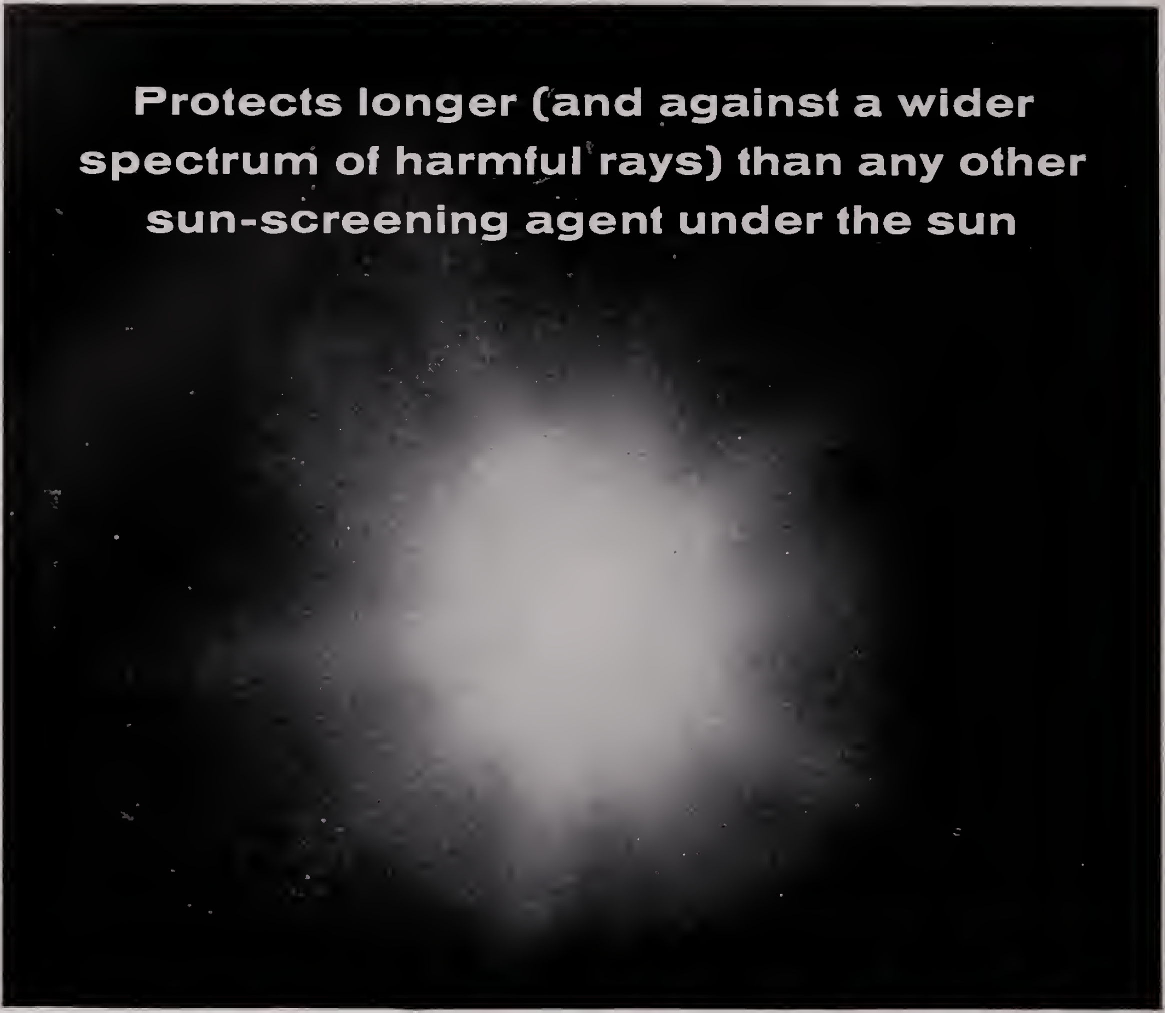
*See Page 1147.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the doctor on the witness stand and doctors by overcoming their aversion to the witness stand, can help to promote a better rapport. The medical and legal professions are both dedicated to rendering service to humanity with full respect for the dignity of man. Working together collectively, solving our mutual problems as colleagues and friends, medicine and law can render far better service to humanity than either of our professions can accomplish separately.

Honorable Donald T. Barbeau*
Minneapolis, Minnesota

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*Presently Judge of the District Court; formerly Chief Judge of the Minneapolis Municipal Court; former Professor, William Mitchell College of Law.

Doctor Wangensteen

THE READERS OF this issue of MINNESOTA MEDICINE* are given a real treat through the publication of Doctor Wangensteen's recent address to the Minneapolis Surgical Society. Here a great surgeon declares his philosophy and beliefs and, in doing so, makes more understandable his ability to stimulate and develop the maximal potential in the young surgeons who have worked under his direction.

For those of us who know, love and admire Doctor Wangensteen, his modest estimates of his own contributions to one of the most productive departments of surgery in the history of medicine, his concise and perceptive review of key contributions to surgical advancement and his sense of direction toward future progress in the surgeons' attack on disease are both impressive and delightful.

It is probably because he has always served in an academic environment that the comments of one who is in private practice of surgery has been solicited.

Doctor Wangensteen has stated emphatically that a man cannot serve two masters at a time. He cannot pursue a productive life as an academic and research-minded individual and also meet the pressing demands of a large clinical practice. Only the suitably endowed and motivated can be effective and happy in the academic environment. The majority must devote themselves to and find satisfaction in rendering the highest quality of surgical care to the public.

The division into two groups should not be absolute. Indeed, the clinical surgeon is essential to good teaching. He is making his contribution toward better surgical care and is keeping himself alert and lessening the gap between new knowledge and its application.

Nevertheless, our skyrocketing progress in the field of surgery and our ability to give the public the benefit of these improvements depend upon the effective marriage of these differently oriented groups. The analogy of marriage carries with it the inevitable misunderstandings, minor quarrels and the requirement of mutual respect inherent to this venerable state.

Rapid changes in the attitude of practice have already occurred and will continue. We can hope that these changes will be evolutionary rather than revolutionary, for thus has surgery and all medicine progressed, keeping what is good and adopting what is new and better.

Must we destroy a system that has done so much for American medicine in order to conform to a pattern more suitable for governmental activity in medicine and completely adaptable to the aims of a large group who wish government to take over completely?

I can best comment on the future of surgery by offering areas of concern, which I am sure are shared by many. In essence we wish to preserve our present system, making what changes are needed to give all the benefit of the best care and preserving the working relationship between teaching, research, and the actual delivery of services.

Naturally, my first concern is the direction in which and the degree to which government will step into the picture, usurping administrative functions best understood and served

Continued

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*See page 1219.

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by physicians. Government encroachment will, of course, affect private practice more than the academic field. Even in the latter, there is cause for alarm; for government, not listening to us and not realizing that it is easier to build schools and laboratories than to find and train competent, research oriented people to man them, threatens to overwhelm our already established and productive teaching institutions.

I am concerned lest the need for highly-trained surgeons exceed the ability of our institutions to utilize the currently accepted best method (dog laboratory) for training them. In such a case, our surgical educators must turn more to the clinical training programs used successfully for so many years. Feeling that the "compassionate graces" are more easily acquired when working with people, there are many surgeons who favor clinical training. Perhaps the laboratory method can be used for those heading for academic careers and clinical training for those planning private practice. A reasonable balance between these two methods is ideal.

With respect to planning careers, I am concerned that trainees shall not be influenced into academic careers unless their interests and aptitudes justify this choice. They should understand that idealism is not exclusively the badge of the academic surgeon; that there are teaching opportunities and immense satisfactions aside from monetary rewards in the private practice of surgery.

The large sums of money poured into our teaching institutions by the government for research, approximately $1,000,000,000 annually, are creating pressures in our medical schools which cause concern for all of us.

The emphasis on research and the consequent demand on the time and thought of our faculties threatens the quality of teaching of our undergraduates. Where this threat is real, it demands the authoritative intervention by departmental heads.

Another effect of the accelerated research programs in American medical schools is the intense, often bitter, competitive spirit it engenders in those participating. Recognition and progress in the academic field depends for the most part on research productivity. There is a temptation, which must be resisted, to publish results and to recommend procedures before they have been thoroughly tried and their value established.

As long as this country can produce its Wangensteens, and it can, the American public is assured of progress in the field of surgery as dramatic as that already achieved. Our danger lies in the threat of revolutionary changes in administering our services to the public. We are obligated to continue our study of these trends, to keep the public informed and hopefully expect the public to defend themselves against damage through the interposition of government between their doctors and themselves.

O. J. Campbell, M.D.
Minneapolis, Minnesota

On the Spot

EVERY PHYSICIAN is used to making decisions affecting the immediate actions of his patients. "You may" and "you must not" are every-day parts of his instructions. In the privacy of the examining room, and supported by laboratory tests and x-rays, his decisions are reasoned and sure. But how secure will he be in a different arena?

Place him instead in the excitement, confusion, and noisy partisanship of an athletic contest. Deprive him of tests and x-rays. Demand a spot diagnosis and an instant decision. Can Johnnie play, or must he be protected?

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entire self and energy to his cause — and not to be deprived for trivial injury. This is the dilemma of the field-side physician.

His decision must be swift and authoritative, fair, and uninfluenced by the honest pressures of the day. He must, then, have guidelines for decision — objective findings and evaluations — thoughtfully prepared for his moment of truth. A series of articles to present such guidelines makes its appearance in this issue of MINNESOTA MEDICINE.* The series is planned under the sponsorship of the Minnesota Committee on Trauma of the American College of Surgeons, through the good services of Dr. Frederick Drill, Minneapolis, and Dr. William Nolan, Litchfield. We commend it to the interest of any doctor who may find himself "on the spot" with an athletic injury.

S. R. Maxeiner, Jr., M.D.**
Minneapolis, Minnesota

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*See Fracture-Trauma Conference Page 1173.

**Chairman, Minnesota Committee on Trauma, American College of Surgeons.

Mathematics and Medicine — Medicometrics

MATHEMATICS IS without any doubt the most exact means of expression and communication that man has today. It is his most inflexible and relentless language. In it he has sought to express all the laws which govern the most primitive mechanics, as well as the infinitely complex cosmos. Mathematics is man's most versatile tool and perhaps one of his oldest.

At the dawn of human awareness man had two choices in the matter of directing his future and acquiring mastery over it. The first was perfecting his own body — by seeking, formulating and expressing reasonably exact laws of vital mechanisms and chemisms* and, in this way, establishing life on a surer basis. The second and more obvious was examing the laws of the universe and reducing them to exact and rigid principles. The most important subsidiary activity was localizing the universal; i.e., building machines in miniature duplication of general universal laws.

The second of these alternatives was the one primitive man chose to follow. He was more interested in constructing a bow and arrow (an attempt to apply primeval mathematical physics to reality) than he was in trying to arrive at an exact understanding and mathematical expression of this vital phenomenon. The physical sciences are, therefore, the more primitive. Early man was more interested in constructing a canoe or a bridge than he was in understanding his own body. The universe was dissected aeons before the organism. This was, perhaps, a very natural thing, for man loves comfort more than he does security of existence.

Modern civilization has been built essentially on a basis of mechanical engineering instead of biological engineering. Our achievements in formulating the laws of astrophysics are phenomenal; but our attempts to reduce biological phenomena to exact mathematical formulas are puny.

The sciences fall into two very broad categories: the biological and the physical. Of the two, the physical sciences are characterized by their mode of expressing their facts and observations in exact and invariable language: mathematics. Mathematical formulas represent tangible facts. The biological sciences have been characterized by a lack of technical language whereby to state their

Continued

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*See Test Your Word Score Page 1167.

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Precautions
Before prescribing, the physician should obtain a detailed history and perform a complete physical and laboratory examination, including a blood count. The patient should be kept under close supervision and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools. Regular blood counts should be made. The drug should be used with greater care in the elderly.

Warning: If coumarin-type anticoagulants are given simultaneously, the physician should watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea and sulfonamide-type agents and insulin. Patients receiving such concomitant therapy should be carefully observed for this effect.

Side effects
The most common side effects are nausea, edema and drug rash. Infrequently, agranulocytosis, generalized allergic reaction, stomatitis, salivary gland enlargement, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia are also possible side effects. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently.

Contraindications
These include: edema, hypertension, or danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. Because of the increased possibility of toxic reactions, the drug should not be given when the patient cannot be seen regularly, when the patient is senile, or when other potent chemotherapeutic agents are given concurrently. Large doses of Butazolidin® alka are contraindicated in patients with glaucoma.

Note: The physician should be fully aware of dosage, precautions, side effects and contraindications as contained in the complete prescribing information.

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fundamental facts. It is for this reason, among others, that medicine cannot be called an exact science, while physics can. The mathematics of biology has not as yet been as fully developed as it might be.

There have, however, been several attempts in the right direction. W. J. V. Osterhout some years ago endeavored to apply quantitative measurements to the processes of life. He attempted to arrive at mathematical formulas to indicate just how much a plant or an animal cell is alive, or how near to the zero point, death. His book, "Injury, Recovery, and Death," is a classic in the nascent science of biological mathematics.

The vital process may be conveniently reduced to a statement: life is the mathematically harmonious relationship among the vital centers of the organism. Physiology has established what these vital centers are, but we have no mathematical formulas which can give us a conception of the complicated interaction among these organs. A calculus of this would, in fact, reduce life to a series of mathematical formulas.

Some time ago Ellice McDonald made an attempt to reduce life to a chemical equilibrium:

$$\mathrm{K} \; \frac{\mathrm{H_2CO_3} \times \mathrm{H} \times \mathrm{S_o} \times \mathrm{E_r}}{\mathrm{BHCO_3} \times \mathrm{CH} \times \mathrm{S_r} \times \mathrm{E_s}}$$

In this formula, K is the protein constant of protoplasm; $BHCO_3$ is the fixed alkali of univalent cations; H_2CO_3, is the fixed acid of bivalent* and trivalent* cations and all anions; OH represents free hydroxyl ions; while H represents free hydrogen ions; Sr represents the reduction part of the oxidation-reduction poise, in the sense of Maxfield Clark; So is the oxidation part of the oxidation-reduction poise of Maxfield Clark; Es represents the sympathetic effect of producing emotions; while Er is the vagus effect producing emotions. In this formula, the equilibrium of life is determined by the protoplasmic constant K. In the upper bracket are the environmental influences producing changes. While this is not a very complete formula, it is an interesting attempt, a groping in the right direction.

Within more recent years Nicholas Rashevsky has been applying mathematical concepts to biology; he is perhaps the first of the modern pioneers in this new discipline. His book, "Mathematical Biophysics," first published in 1938 and since then revised and enlarged in several successive editions, is a pioneer effort in an entirely new direction. Rashevsky has applied mathematical interpretations to the theory of embryonic development, the theory of cancer, cell division, perception of visual processes, learning, logical thinking and abstractions, among many others.

It will be many years before we have a theoretical biology comparable to a theoretical physics. The heartening thing is that very encouraging beginnings are being made.

Editor's Note: Progress is being made in all fields of medicine. Why not medicometrics? Perhaps some day we can each write our own eugenic pedigree into the formula.—C.O.R.

Edward Podolsky, M.D.
Brooklyn, New York

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*See Test Your Word Score Page 1167.

Astrology and Medicine

The planet Mercury, when malefic, predisposes to nervous disorders: aphasia, amnesia, headaches, neurasthenia, and other pathologies involving the brain and nerves. The occult Mercureal influence is continuously operative in human destiny even though the planet itself is seldom visible to the naked eye because of its close proximity to the sun, whose dazzling light obscures the small satellite.

On rare occasions, however, Mercury can be detected as morning or evening star, preceding the rising or following the setting sun.

Pleasant words are as an honeycomb, sweet to the soul, and health to the bones.
— Proverbs 16:24

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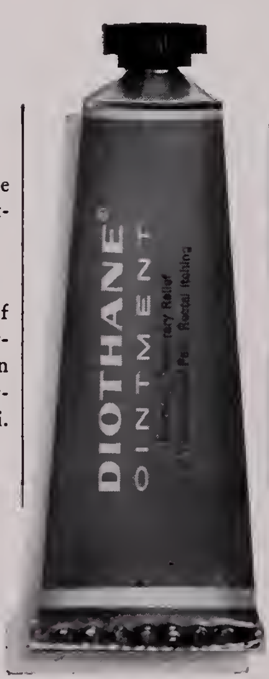

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Test Your Word Score

Chondriospheres — *a large or aggregated spherical body* (page 1129).

Thrombocythemia — *abnormally small number of platelets in the circulating blood* (page 1131).

Collimation — *localization of tumor by selective pickup gamma rays from injected radioactive substance* (page 1138).

Sisyphus — *Gr. Myth. King of Corinth, condemned in Hades to roll a huge stone up a hill, which constantly rolled back* (page 1149).

Chemisms — *chemical action or influence* (page 1163).

Bivalent — *possessing twofold combining power* (page 1165).

Trivalent — *possessing threefold combining power* (page 1165).

Perseverate — *constant repetition of a meaningless word* (page 1184).

Surrogate — *substitute, deputy,* (page 1187).

Scleroderma — *thickening of skin caused by thickening of fibrous tissue — hidebound disease* (page 1194).

Valleculae — *depressions or furrows* (page 1195).

Fasciculations — *involuntary contractions of muscle groups or fibers, coarser than fibrillation* (page 1200).

Opisthotonos — *tetanic spasm in which the head and heels are bent backward* (page 1206).

Oculogyric — *pertaining to movement of the eye about the anterposterior axis* (page 1206).

Cyclothymic — *cyclic insanity — manic-depressive psychosis* (page 1207).

Ataractic — *pertaining to detached serenity of the mind* (page 1208).

Diapedesis — *passage of blood elements through intact vessel walls* (page 1222).

Letter to the Editor:

In a recent issue of MINNESOTA MEDICINE[1] attention was drawn to Troisier's sign, the presence of an enlarged left supraclavicular lymph node indicative of advanced carcinoma of the stomach. My interest was aroused because I had been taught that this was Virchow's gland, in honor of the great German pathologist, Rudolf Virchow (1821-1902), the founder of cellular pathology, creator of the doctrine of embolism, and public official in Berlin. I was not familiar with Troisier.

A little research, with the assistance of Mr. Thomas E. Keys, Librarian at the Mayo Clinic, disclosed that Charles Emile Troisier was an excellent clinician and pathologic-anatomist of Paris who lived from 1844 until 1949. One of his major contributions, in 1874, was a study of the spread of cancer through the lymphatics. He devoted special attention to cancer of the thoracic duct and to the involvement of the supraclavicular lymph nodes. This involvement may indicate a primary cancer of the thoracic cavity, the stomach, intestine, liver, pancreas, kidney, uterus or uterine adnexae.

Continued

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Precautions: Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of preexisting symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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A woman, aged 72 years, consulted me because of pain in the abdomen of two weeks duration. The pain radiated into the chest and to the interscapular area. On examination, enlarged lymph nodes were found in the left supraclavicular area and there was a hard, movable mass in the left upper abdominal quadrant. Pathologic examination of the excised left supraclavicular lymph node revealed rapidly growing metastatic adenocarcinoma. The sign of Troisier was valuable in establishing the diagnosis and the patient was spared an exploratory laparotomy.

On many occasions this sign has been useful and revealing to me. I feel indebted to the distinguished French physician whose name it bears and to MINNESOTA MEDICINE for bringing its proper identity to my attention.

H. B. Neel, M.D.
Albert Lea, Minnesota

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2. Chanannag, M. G.: Ganglion de Troisier et Chirurgie. Bull et mem Soc de Chir de Paris 47:171, 1921.
3. Laverau: Charles Emile Troisier 1844-1919. Bull Acad de Med 3 S. Vol. 82:490, 1919.

Editor's Note: I think we both were right. It is Troisier's Sign and Virchow's Node.

The Editor's Soliloquy

Medicare

Perhaps we are on the eve of a new philosophy wherein the social state must be given the responsibility of paying all hospital costs for all people, all medical bills for all people, all drugs for all people. What is there to stop this line of thinking from extending to all items in the drugstore and finally to all commodities, no matter what, for all people — in accordance with their whims and not their needs.

By removing the incentive for personal protection, in a job well done and accordingly remunerated, may we hope that government intervention under the guise of benevolence will not be the opening wedge to initiate decay of the greatest medical progress of all time. Now that we have it, it is incumbent upon us to maintain our equanimity and continue to provide honorable, ethical, high-grade medicine to all our patients.

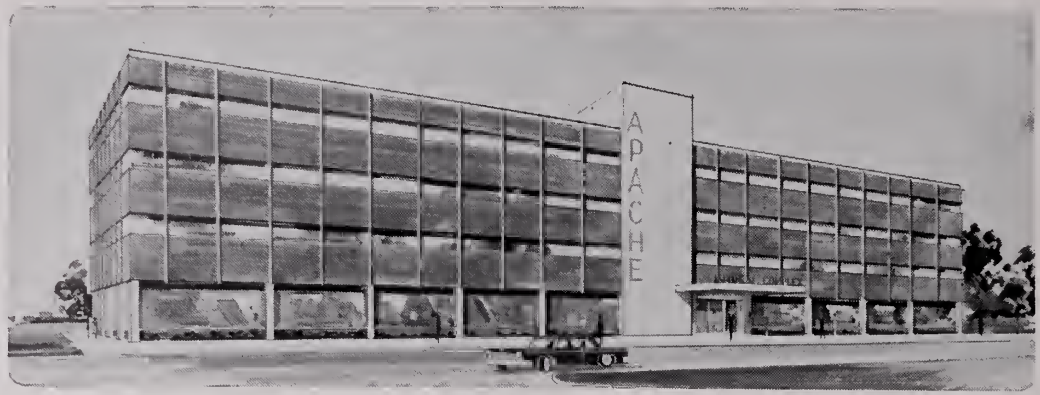
— Carl O. Rice, M.D.

President's Letter continued from page 1123.

gestions could make the AMA a more efficient, yet representative, organization better able to serve the physicians of this country in an adequate manner. If this is desirable at a national level, it is equally so at the state level. The Committee on Permanent Evaluation of the Minnesota State Medical Association should be encouraged to continue its activity. The essence of the whole thought is to advocate the selection of capable representatives and to allow them to function in a framework designed for efficient operation.

J M Stickney M.D.

J. M. Stickney, M.D.
President
Minnesota State Medical Association



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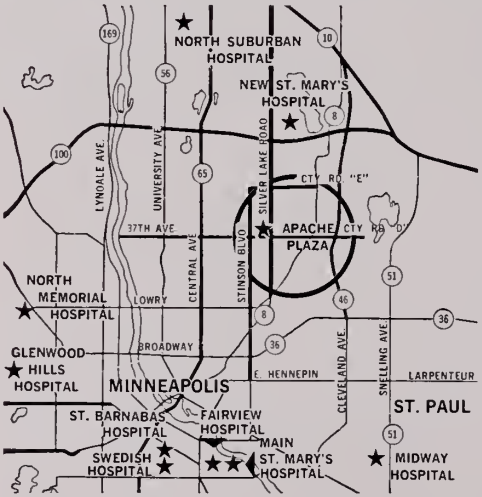
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Curbstone Consultation

de Quervain's Disease

QUESTION: I am unclear as to the nature of the pathology in de Quervain's disease. Is the management similar to that for a tenosynovitis elsewhere?

ANSWER: De Quervain's disease is a stenosing tendovaginitis rather than a tenosynovitis. A tenosynovitis is essentially an inflammation of the cellular mucin-producing lining membrane of the fibrous tissue tube — vagina — through which the tendon glides. Treatment of the acute process in such cases usually responds readily to immobilization and hydrocortisone injections directed into the space between the tendon and synovial lining of the tendon sheath.

The stenosing tendovaginitis in de Quervain's disease involves the abductor longus and extensor brevis tendons of the thumb. Stenosing tendovaginitis in contradistinction to tenosynovitis, involves the fibrous wall of the tendon sheath at special regions, rather than the lining synovium of the entire sheath. It occurs where the tendon passes through a fibrous ring or pulley, usually located over bony prominences. In the case of de Quervain's disease this is at the radial styloid process of the wrist. Due to proliferation of the fibrous tissue at this site there is encroachment on the tendon as it passes through the fibrous ring in that region. Finally the tendon becomes constricted by the hypertrophied ring. Definitive treatment for this condition consists in longitudinally incising and partially excising the thickened tendon sheath at the affected site.

Drugs Causing Hepatitis

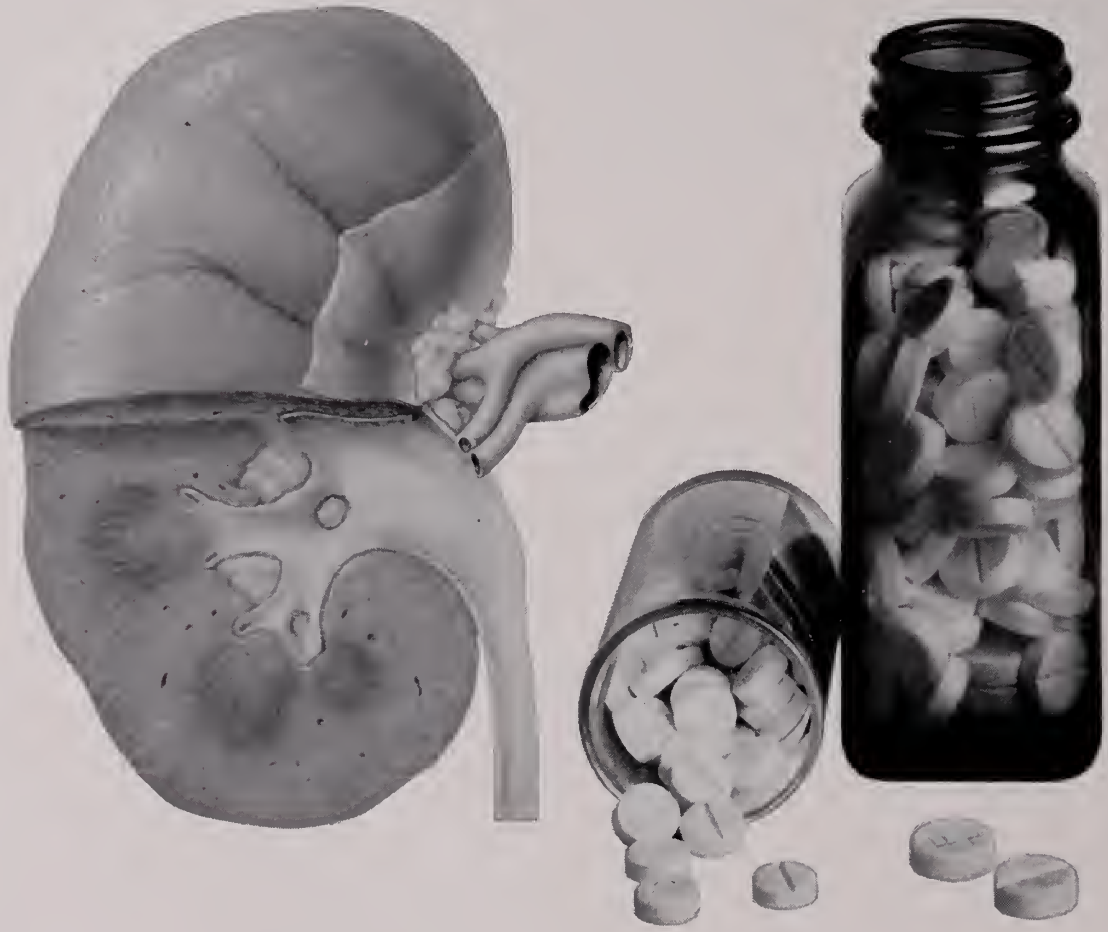
QUESTION: What are the most common drugs causing hepatitis?

ANSWER: Probably the drugs most commonly causing trouble today are the phenothiazine tranquilizers, PAS and the anabolic steroids. The number of viral hepatitis-like reactions, although very serious, is small.

Fenton Schaffner, M.D.
Mt. Sinai Hospital
New York, New York

We can no more escape choosing than we can escape the consequences of our choice. — Cliff S. Emeny, Rule of Law, Freeman

at Merck Sharp & Dohme...



The development of chlorothiazide and probenecid were events of major importance, but perhaps even more important for the future was the Renal Research Program by which they were developed. When Merck Sharp & Dohme organized this program in 1943, it was expressing in action some of its basic beliefs about research:

- Many problems connected with renal structure and function were still undefined or unsolved. The Renal Research Program would begin its basic research in some of these problem areas.
- From knowledge thus acquired might come clues to the development of new therapeutic agents of significant value to the physician.

For example, the Renal Research Program put fifteen years into this search before chlorothiazide became available. But because these years had first led to a greater understanding of basic problems, the desired criteria for chlorothiazide existed before the drug was developed.

Along with other research teams at Merck Sharp & Dohme, the Renal Research Program continues to add new understanding of basic problems—understanding which will lead to important new therapeutic agents.

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where today's theory is tomorrow's therapy

Fracture–Trauma Conference

Management of Ankle Injuries Sustained in Sports

The doctor on-the-scene has the best opportunity to make an accurate diagnosis and must ultimately determine if and when the athlete with an ankle injury may return to the game. With any injury to the ankle, it is well-advised to bring the player to the side lines, not allowing him to bear weight on the injured extremity. The shoe and taping should be removed, and careful examination carried out. Often it is helpful to examine the normal ankle as well, in order to compare relative ranges-of-motion and stability of the various ligaments.

Quigley[1] has suggested that sprains be graded in severity from i to iv; grade i being the least degree of injury and grade iv being complete rupture. With grade ii sprains properly treated in a cooperative patient, the injury was sufficiently healed to allow full participation in contact sport about eight days following injury.

Athletes in contact sports should have their ankles wrapped for practice sessions as well as in game conditions. Rarick[2] reported that the greatest support was achieved with the basketweave and the combination stirrup and heel lock wrapping. The least support was given by the standard basketweave. He found that as much as 40 per cent of the supporting strength of the strapping was lost after exercise; nonetheless, the remaining 60 per cent of strength certainly affords protection.

Diagnosis

Severe Injuries

In severe injuries involving fractures or dislocations for the first 30 minutes or so the patient usually has very little pain, unless the tibial nerve is being severely stretched. Before pain, hematoma, and swelling occur, the team physician has a "golden opportunity" to manipulate the foot and ankle back to normal alignment. If the foot and ankle are displaced laterally and posteriorly, as is usually the case, the foot should be pulled anteriorly on the tibia and held in inversion. A bulky pressure dressing, using sheet-wadding or cotton held in place with a 6-inch ace bandage, will immobilize the injured part very well. The patient can then be transferred in relative comfort to a hospital for x-rays and further care.

Minor Injuries

Only in minor injuries where there is found to be full range-of-motion, good stability, and no significant pain with stress placed on the various ligaments, should the team physician consider allowing that player to

Continued

return immediately to the game. If there is evidence of hematoma formation, a grade ii, iii or iv sprain must be suspected, and the player must be prohibited from further participation on that particular day. The stability of the collateral and the anterior tibiofibular ligaments should be tested and compared to the stability on the uninjured side. If external rotation of the foot on the tibia causes pain over the deltoid ligament or a sensation of crepitus over the distal fibula, or if there is undue laxity of any ligament, that patient needs further evaluation at the hospital including x-rays.

X ray Examination

X-rays should be taken in three views; these include an AP with the toes straight up, an AP with the extremity internally rotated 20 degrees, and a lateral view. Stress films can be taken; but because of wide variation in the normal talar-tilt angle, a talar tilt of less than 23 degrees is not a reliable indication of rupture of the fibular collateral ligaments.[3] External rotation stress films are of value in determining the status of the deltoid ligament.

Treatment

Ankles which have sustained grade i sprains should be rewrapped if the athlete is to return to participation immediately. After the game, the extremity should be elevated and ice-packed for the first 24 hours. Following that, whirlpool and active exercises will help shorten the period of rehabilitation, will help regain lost range-of-motion, and will provide mild analgesic during the exercise.

Treatment of grade ii and iii sprains should include immediate pressure dressing, ice-packing, elevation, and rest. For weight bearing, the ankle should be supported with either tape strapping or a short-leg walking cast. The patient should be kept on crutches with partial weight bearing until he can walk without pain or limp. This will often take anywhere from seven to twenty-one days. Active range-of-motion can be started when he experiences no pain with the range-of-motion exercises. Under no circumstances should there be passive range-of-motion or heavy massage. Procaine injection into the ankle so that exercise can be carried out is mentioned only to be condemned.

Grade iv sprains are diagnosed when x-rays taken with external rotatory stress on the foot show lateral subluxation of the talus; this means that the deltoid ligament has been ruptured, possibly along with the distal anterior tibiofibular ligament. If there is a diastasis between the distal tibia and fibula, the interosseous ligament has also been ruptured. Grade iv sprains should be treated with a long-leg cast following reduction, the knee being flexed about 20 degrees. The cast should be left in place for six weeks without weight bearing. Post-casting x-rays definitely must be taken to rule out lateral displacement of the talus occurring during cast application. Spiral fractures of the distal fibula without lateral subluxation of the talus during external rotatory stress films, may be treated like grade iii sprains.

Frederick Drill, M.D.
Minneapolis, Minnesota

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Tumor Conference

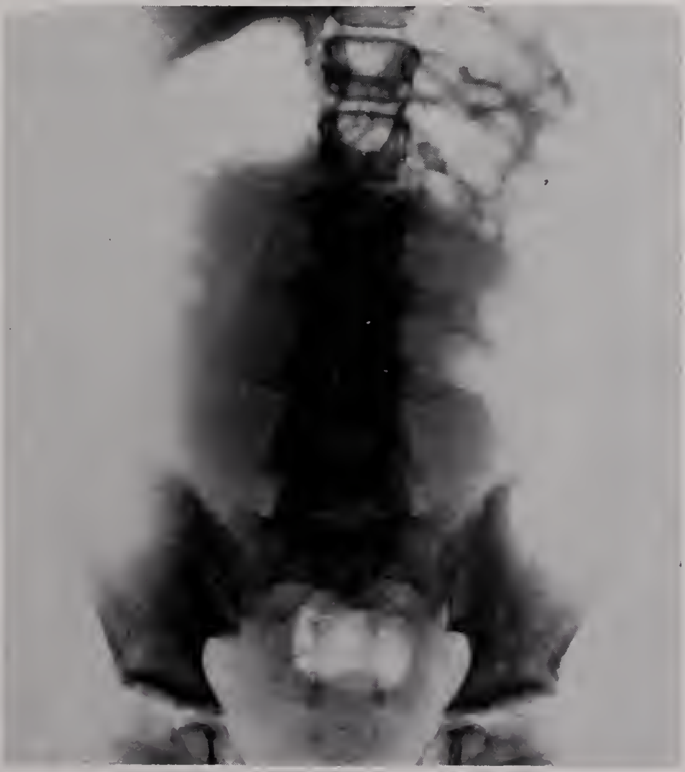
Malignant Ovarian Teratoma in a Nine-Year-Old Girl

The development of a malignant tumor in a child is a deeply distressing problem to both the family and the doctor. Because the child has a period of future growth, certain modalities of treatment are not applicable. The following case history illustrates this problem:

Case History

A nine-year-old white girl was admitted to Swedish Hospital on July 11, 1964, with a three-day history of lower abdominal pain and distension. She had had difficult, infrequent and bulky stools since birth. She had had urinary tract infections twice during the preceding year. A doctor, who examined her at the onset of her pain, thought she might have a fecal impaction as the cause of her abdominal distension; but enemas gave no relief.

On admission, she was not seriously ill. There was moderate abdominal tenderness in the left lower quadrant and a mass extending up to the umbilicus on the left and somewhat lower on the right. X-rays revealed a 22 cm. mass in the lower abdomen. The left ureter was displaced anteriorly and to the left. The intravenous urogram and colon X rays were otherwise normal. A chest X ray was also normal. Hemoglobin was 10.7 grams and the sedimentation rate 68 mm./hour. The white blood count decreased from 12,600 to 8,600 in 36 hours.



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Exploratory laparotomy revealed a large, somewhat cystic mass with an 8 cm. irregular, nodular, yellowish-gray area on one side. There was edema of the broad ligament but no apparent spread of the tumor. The uterus and right ovary were normal. Her postoperative course was uneventful. The first microscopic sections resembled a dysgerminoma, but additional sections proved the tumor to be a malignant teratoma.

Although malignant teratomas are somewhat sensitive to cobalt therapy, the dose required is so large that there would have been marked effects upon the epiphyseal centers of the lower spine, pelvis, and femurs. Because of her young age, this modality would likely have left her severely crippled.

Borrowing from the experience of "second look procedures" in management of carcinoma of the colon, a second laparotomy was performed on October 12, 1964. Biopsies were taken from adhesions to the left abdominal wall, left iliac lymph node, the stump of the left infundibulopelvic ligament and a small nodule on the right ovary. No residual tumor was found either grossly or in any of these microscopic sections.

The girl has remained well and one year after surgery shows no evidence of recurrence.

Discussion

Pathology

Teratomas of the ovary are usually solid, smooth and well encapsulated. About 12% are bilateral. Solid teratomas are most frequently found in young women. The peak incidence is during the second decade of life. Teratomas comprise 15% of ovarian tumors in children. The embryonal and undifferentiated tumors are rapidly fatal, with death usually occurring during the first year.[1]

Most teratomas of the ovary are benign. Kent and McKay[2] reported an incidence of 1% malignancy. Five of their series of 443 cases were malignant. Peterson,[3] in a collected series of 8,038 dermoid cysts, found 147 with carcinoma, an incidence of 1.8%.

Most of the lesions are squamous carcinoma, but other types of tumor have been observed, such as choriocarcinoma, carcinoid tumors and struma ovari (thyroid carcinoma).

Treatment

Gross[4] reported four teratomas in a series of thirteen cases of malignant tumors of the ovary in Boston Children's Hospital. Two died of metastasis within a few months. One was alive and well seven years later and the other fourteen years later.

The best hope for a cure is early gentle surgical removal of the tumor. Cobalt therapy and other cancericidal agents are of limited value. If the patient has attained her growth, cobalt therapy should be used postoperatively.

The extensive radiation required for this radio-resistant tumor would likely result in severe deformities of spine, hips, and pelvis in the actively growing child. Garland,[5] in citing from Wittenburg and Newhauser, states that "almost invariably a tissue dose of over 2,000 r produces discernible bony alteration. This effect is related directly to the dose delivered to the spine and related inversely to the age of the patient."

If the malignant teratoma is apparently completely removed, postoperative radiation is not justified. A "second look" laparotomy in three months is suggested as a means of detecting and removing recurrent tumor.

Summary

Malignant teratoma of the ovary is a rare tumor occurring most frequently during the second decade of life.

It is best treated by careful complete surgical removal.

Postoperative radiation is of limited value and used only after body growth has been attained.

A "second look" laparotomy may be used to control local recurrences.

Elmer J. Martinson, M.D.
Wayzata, Minnesota

Patient referred by Dr. R. G. Swenson of North Branch, Minnesota. Dr. Felix A. McParland, Minneapolis, Minnesota, pediatric surgery consultation.

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ANSWER TO WHAT'S YOUR DIAGNOSIS

(From page 1152)

Cryoglobulinemia. The test — a viscid layer forms when the serum is cooled to 4 degrees Centigrade, and redissolves when the serum is warmed. The exact etiology of the cryoglobulinemia in this case is, as yet, undetermined. Twenty-five per cent will be essential, 50 per cent will be a multiple myeloma, and the other 25 per cent will be divided among chronic liver disease, lymphomas, collagen diseases, and other factors.

The Foodic Again*

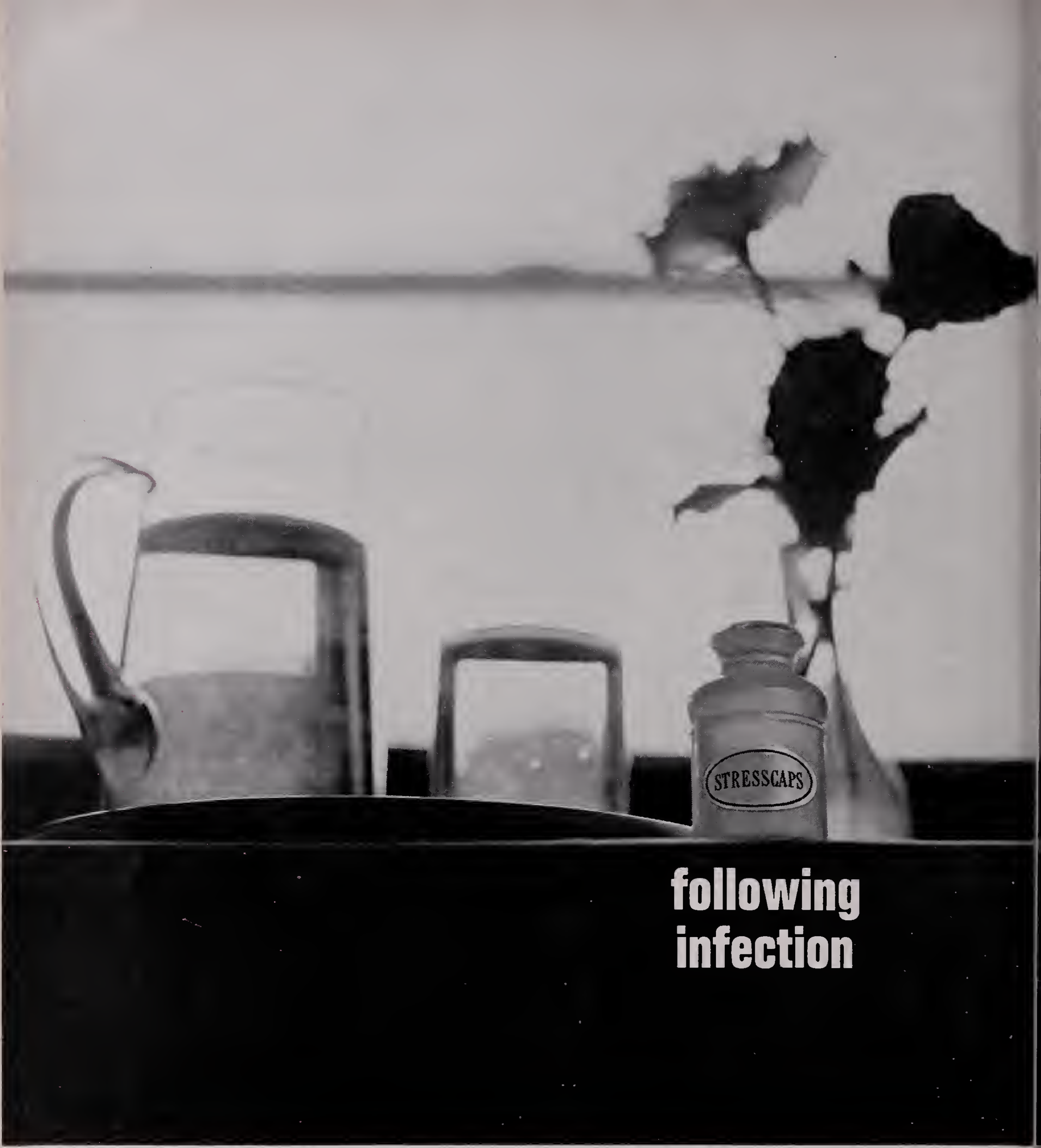
A nice, convenient classification of obesity might be first, just mildly obese, which should likely refer to the pleasingly plump individual who is still pretty smoothly proportioned, does not stick out too much here and there, and who may realize, I hope, that it is better to prepare and prevent than to repair and repent.

The second degree of obesity could be termed the stout or corpulent type who bulges fore and aft, and who half talks with his belly which bobbles around like jelly when he laughs. He usually wheezes and puffs, is often knock-kneed, is forever trying to impress his audience of his light-footedness in spite of his flat-footedness.

And at last, there is the really fat individual, whose chins are a part of his chest, who can't speak for fear of over-exerting himself, and if he does happen to move, he flows. He has given up trying to be thinner even next year, worries only about where the ham and potatoes are to come from tomorrow, and has given up the inspection of his hidden bodily acres and acres that he can view only with a mirror.

— F. William Saul, M.D.: Pink Pills for Pale People

*See Minnesota Med 46:663, 1963.



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Niacinamide	100 mg.
Vitamin C (Ascorbic Acid)	300 mg.
Vitamin B_6 (Pyridoxine HCl)	2 mg.
Vitamin B_{12} Crystalline	4 mcgm.
Calcium Pantothenate	20 mg.

Recommended intake: Adults, 1 capsule daily, for the treatment of vitamin deficiencies. Supplied in decorative "reminder" jars of 30 (one month's supply) and 100 (three months' supply).

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Neuro-Pediatrics Conference

Sublingual Thyroid and Acquired Hypothyroidism*

Dr. Samuel Rotenberg:** This white female was born October 22, 1958, of a pregnancy during which the mother had pneumonia in the first trimester. The delivery was normal and the child breathed and cried immediately. The birth weight was 5 pounds, 11¾ ounces, and the neonatal course was normal. At seven months of age, the infant had an upper respiratory infection, and at 13 months of age an episode of otitis media. At this time, her hemoglobin was noted to be 8.5 grams per cent. She was started on iron therapy, and two months later her hemoglobin was 10.8 grams per cent. She has also been given Imferon® injections, but without any change in her hemoglobin. During the next two years, she had multiple upper respiratory infections, otitis media and several episodes of bronchitis. A persistent anemia was noted on these visits and was treated with oral and intermuscular iron. Her hemoglobin ranged from 8.5 grams per cent to a high of 11 grams per cent in September, 1964.

She had received her original series of diphtheria-pertussis-tetanus immunizations in 1959 and Sabin polio vaccine in 1960. In September, 1964, she received her booster diphtheria-pertussis-tetanus shots and her smallpox vaccination; her tuberculin test was negative. The mother, who felt that the child was no different from other children, wanted her to go to school, even though she was shy and withdrawn.

In November, 1964, a conference was held with the parents and the school, and it was decided that a thorough medical examination should be performed because of the child's small height and her shy and withdrawn behavior.

Miss Helen Engelbretson:†

Subsequently the family moved to Omaha for a year and another conference was held prior to the child's starting school in the fall of 1964. As the mother felt that her little daughter was "ready for school," an interview was held with Mr. Rasmussen, a psychologist in the Robbinsdale

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*Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatric conferences are held the first and third Wednesdays of every month from 3:15 to 4:15 p.m. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Robert W. ten Bensel, in Pediatrics, and Dr. Robert Soll, in Adult Neurology. Held on Wednesday, February 17, 1965, at 1 p.m.

**Private Physician, Minneapolis, Minnesota.

†Social Worker, Robbinsdale Public Schools.

Continued

School System. On the basis of his studies, she was placed in a special kindergarten class with Mrs. Lindstrom as her teacher.

Mrs. Maxine Lindstrom*

The patient had had no prior kindergarten experience, and physically she was not on a par with the rest of the children in the class. The only emotion she expressed was on the first day of school, when she cried upon debarking from the bus. Otherwise, she has responded and worked well in class; however, she has shown no enthusiasm for her work, and her small size has set her apart from the rest of the students. At the parents' conference in November, it was learned that she did not talk until she was four years of age, and the mother felt that perhaps she "babied her too much." The parents were then aware of the need for further medical evaluation and thus the referral back to Dr. Rotenberg.

Dr. Mark Mathison**

In the Pediatric Outpatient Clinic in December, 1964, additional history revealed the child's developmental milestones to be as follows: she followed objects with her eyes at two months, rolled over at six months, sat without support at eight months, and walked at one year of age. Single words were spoken at 18 to 21 months, and short sentences at four years. The mother first noted a change in the patient at age two, when she seemed slow in

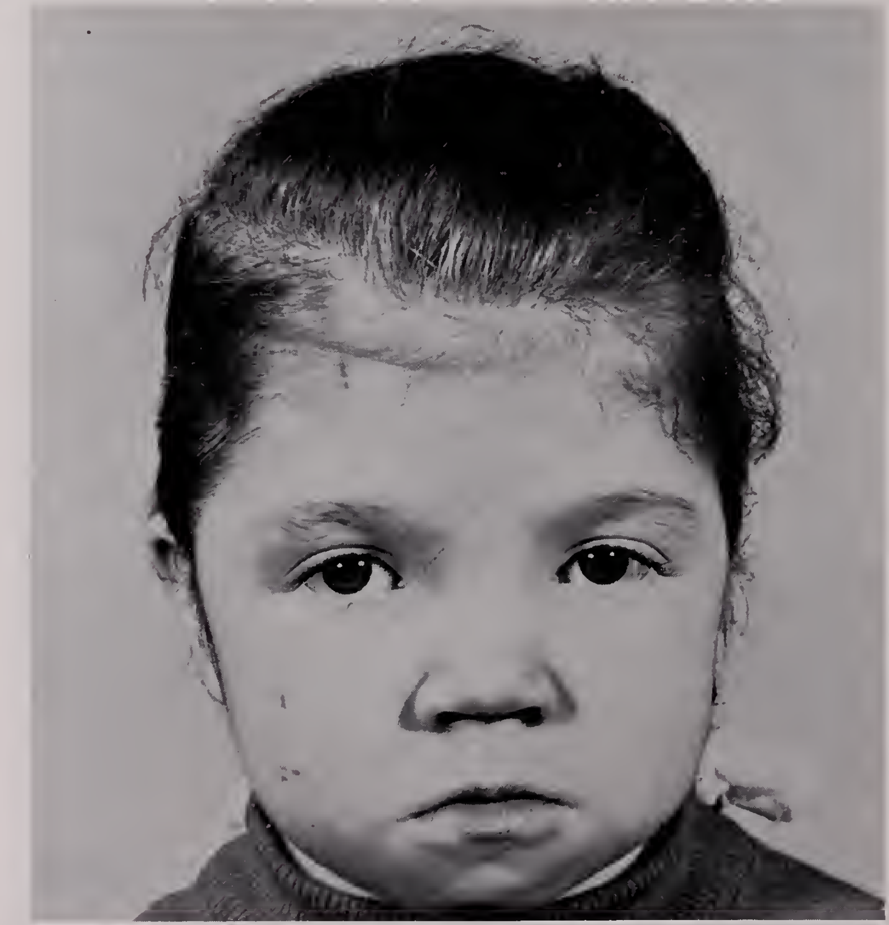

Fig. 1 — Acquired hypothyroidism with apathic facies and low hair line.

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*Teacher, Robbinsdale Public Schools.

**Senior Medical Student, Comprehensive Clinic Program, University of Minnesota Medical School.

speech and "very quiet." The patient has always been a poor eater and has been constipated throughout her life. The mother has also noted that her hair and skin have been rather coarse compared with those of the other children in the family.

Physical Examination

Examination showed a pale, very shy, apprehensive female who was small for her age. Her height was 93.5 cm. and her weight, 15.6 kg., both of which were far below the third percentile. Her hair was very coarse and extended down over her forehead, and a flattened nasal bridge was noted.

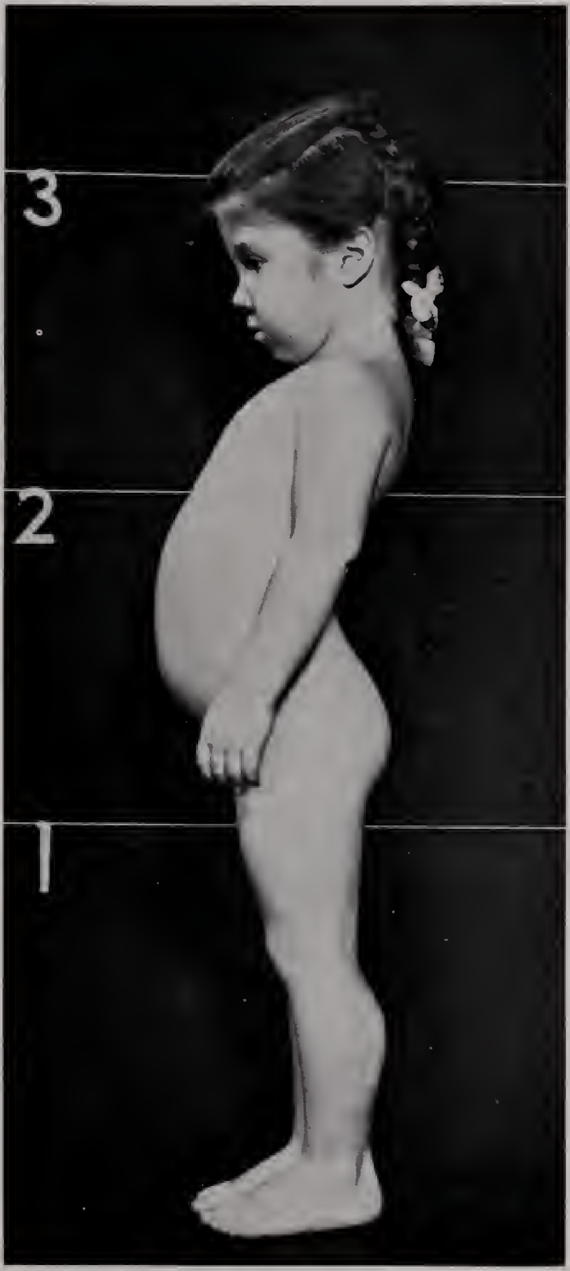

Fig. 2 — Acquired hypothyroidism. Note protuberant abdomen, flattened nasal bridge, and increased hair on arms and back.

Continued

The thyroid gland was not palpable. Her skin was very dry and there was dark, coarse hair on her arms. A grade I/IV heart murmur was heard, interpreted as functional in nature. Her liver was palpated 2½ cm. below the right costal margin and no spleen was felt. The neurological examination showed a very slow response in the deep tendon reflexes. Mental examination was difficult because of her shy, withdrawn nature.

She was admitted to the University of Minnesota Hospitals in February, 1965, for further thyroid evaluation, after protein-bound-iodine of 2.3 mg. per cent was obtained. Other studies in the hospital showed a T_3 of 8.9 micrograms% (10-14 micrograms%, normal range); radioactive iodine uptake of 5.7% (normal — 20-40%), and a bone survey consistent with hypothyroidism. Her serum carotene was 208 mg.%; vitamin A, 35 mg.%; serum cholesterol, 282 mg.%, and hemoglobin 11.8 grams%. A thyroid scan showed a sublingual thyroid gland.

A muscle biopsy was performed which was histologically normal. Electromyography showed a pattern consistent with myopathy, affecting proximal as well as distal musculature.

Dr. Richard Chilgren*

A diagnosis of acquired hypothyroidism was considered. Her weight chart shows that she was in the 50th percentile until two years of age; at that time her weight leveled off and has shown essentially no increase (Figure 3), which indicates that she does not have complete absence of thyroid. To further establish this fact, the thyroid scan was performed and showed a picture of the lingual thyroid, which is quite rare. Dr. Henning Anderson of Sweden feels that this condition is more common than previously thought, because the linguinal area is usually not included in the thyroid scan. Embryologically,[1] the thyroid has its origin at the base

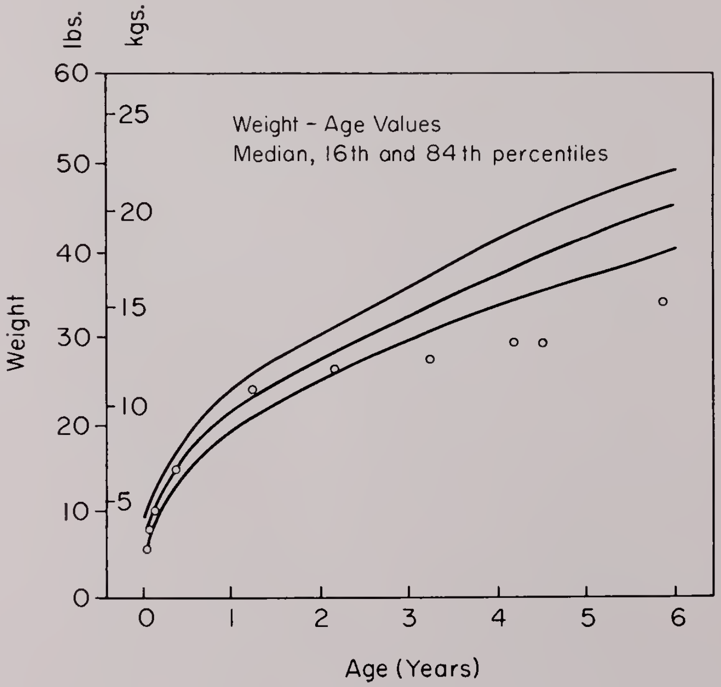

Fig. 3 — Weight chart of patient with acquired hypothyroidism, showing fall-off at 1-2 years of age.

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*Pediatric Metabolic Resident, University of Minnesota Medical Center.

of the tongue and then migrates to a position in the anterior portion of the neck in front of the trachea. When the gland does not migrate and stays in the sublinguinal area, it functions for a while and then stops after one to two years. Thus, this condition is different from cretinism, in which children are born with no thyroid. Her bone age at the present time is less than that of a one-year-old child and her height and weight correspond to those of a three-year-old child. This is also consistent with a diagnosis of acquired hypothyroidism.

Treatment

Presently she is being treated with desiccated thyroid, starting at a very low dose of ½ grain, which will be gradually increased by ¼ grain each week, to 2 to 4 grains eventually. The end point of therapy will arrive when the protein-bound-iodine enters the range of 5.5 to 7 mg.% and when she shows a clinical response. Hopefully, her intelligence will increase, but this has not been assured to the parents. Usually the prognosis is good in this condition; we expect a longer growth phase and she should approach normal height, though there may be some doubt that she will completely attain it.

There was no evidence of any adrenal or pituitary dysfunction and her electrolytes were normal. A thyroid-stimulating-hormone test would not change the therapy and, as with the SU 4885 test, was not felt to be indicated. Thyroid-stimulating-hormone for treatment is an interesting idea but desiccated thyroid remains the desired treatment.

The toxic signs of the medication that would be helpful to alert the school officials are: (1) severe agitation and irritability which may occasionally, but rarely, result in unconsciousness and seizure manifestations; (2) ravishing hunger; (3) profuse sweating, and (4) rapid heartbeat. If any of these signs are observed in the patient, Dr. Rotenberg should be contacted.

Dr. Robert ten Bensel:

Chronic normochromic, normocytic anemia is a not uncommon finding in acquired hypothyroidism and is unresponsive to iron. The nature of this anemia is not known; but thyroid is probably important in red-cell metabolism.

Mrs. Mary Cordingley:*

Both the mother, age 34, and the father, age 38, are slow-moving, slow-speaking, and rather passive in attitude. The father is a foreman of a potato-processing plant. Upon his recent return to his company he was unable to get group insurance because of the patient.

Other children in the family include a fifteen-year-old boy and twins, thirteen years old. Although there have been no special behavior problems in school, one of the twins has some academic difficulties and tests in the low-normal range. The oldest of the boys is doing extremely well. Their attitude toward the patient is one of solicitude.

Perhaps in visualizing the patient's potentials, one should not ignore the slow, passive attitudes of the parents and the limited ability of the low-normal twin. Such familial patterns may serve as limitations to the patient.

Heretofore, most of the plans made by these parents have been results of suggestions by others, indicating their basic trust and willingness to

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*Social Worker, University of Minnesota Medical Center.

Continued

co-operate. It is therefore important that these parents have an exact interpretation of the expected progress and an evaluation of possible changes in their child's development. Because of their literal interpretations and high expectations of improvement, these parents may be likely to expect more than is physically possible; therefore idealistic projections should be kept to a minimum.

Dr. Paul Moe:*

In examining the patient the most striking finding was her mental torpor. She had very little concept of numbers but could count to five. She knew simple body parts; but in general her mental ability was judged to be at an 18 to 24-month level. On neurological examination the only abnormal finding was her "hung up" reflexes.

Mental Development

The nervous system is often affected in hypothyroidism, and affliction may express itself in a variety of ways.[4] In adults, paresthesias, ataxia, headaches, seizures and hearing deficits are observed. The adult usually retains his intellect, whereas the infant may show severe impairment, especially when there is congenital absence of the thyroid gland. The question from the neurological point of view is: how adequately will her intelligence develop. Wilkins[3] feels that in acquired hypothyroidism 40% of the children will have an I.Q. greater than 90 and 6% will have an I.Q. of less than 50. Williams[2] feels that of children who have acquired hypothyroidism with onset between one and two years of age, approximately 90% will reach an I.Q. in the normal range. It is important to remember that the most meaningful evaluation of this child's intelligence will be approximately two years after treatment has been started. Early, there may be scatter in the intelligence testing, due to psychological reactions to therapy.

Myelination of Nervous System

In the child who is born without a thyroid gland it has been shown that thyroid is important in myelination of the nervous system, impaired at birth. Myelination is usually completed in the first 24 months of life; therefore this child should have little permanent intellectual impairment. In general, her prognosis should be relatively good and she should achieve well.

Dr. Harold Ireton**

The child was found to be almost totally nonverbal. Responses were indicated by shaking her head and by performance on nonverbal test items. At the time of testing she was six years, four months old. On the Binet nonverbal tests she demonstrated a mental age somewhat under five years (M.A., 4-8, estimated I.Q., 70). She showed some tendency to perseverate† on this test. On the Draw-A-Man Test, she performed on approximately the same level (M.A., 5-0), but her drawing included unusual distortions (the body was drawn within the outline first drawn as a circle for the head). On the Peabody Picture Vocabulary Tests, her performance was considerably more retarded (M.A., 3-1, I.Q., about 50). The results of testing, especially her limited vocabulary, indicated general mental retardation. Her limited language use is probably a reflection of such retardation rather than of "shyness." The mother's report on the patient's general social adjustment (Vineland Social Maturity Scale) indicated approximately average functioning for her age, except in the area of communication; but her report may be somewhat exaggerated.

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*Pediatric Neurologist, University of Minnesota Medical Center.

**Clinical Psychologist, University of Minnesota Medical Center.

†See Test Your Word Score Page 1167.

Both parents recognize her speech limitations, but the father appears relatively more aware of the degree of her intellectual limitation. Neither parent shows any significant psychiatric disturbance; but the father seems to be quite introverted, a lethargic type of person, who is probably chronically somewhat depressed. Unless there is significant change in the rate of mental growth, the child's education should continue at a slowed pace, geared to her mental age with special class education. At the present time, specific remedial reading or similar therapy does not seem indicated. Even though there is medical optimism about the reversibility of her general condition, this should not be communicated to the parents. Failure of intellectual improvement under such expectations could be psychologically damaging to the parents and interfere with meeting the child's present needs.

Final Recommendations of the Conference

1. Dr. Rotenberg will maintain his role for the primary medical responsibility in this case.
2. The patient will be seen in the Endocrine Clinic on a weekly basis until her thyroid medications are adequately adjusted. She will then be seen at one to six-month intervals for a period of time, and then yearly to judge the effect of therapy.
3. Close communication will be maintained between the University Hospital, Dr. Rotenberg and the school, regarding progress and changes in her condition.
4. Psychological testing should be performed by the school in approximately two years in order to re-evaluate her educational situation at that time.
5. It was generally agreed upon that counseling of the parents should maintain a positive attitude, but one should move slowly in prognosticating her eventual intellectual status.

Robert W. ten Bensel, M.D.
Moderator
University of Minnesota Medical Center

Those participating in the conference include: Dr. Samuel Rotenberg, Private Physician; Dr. Mark Mathison, Senior Medical Student; Mrs. Leila Hemstock, School Nurse, Robbinsdale Public Schools; Mrs. Maxine Lindstrom, Teacher, Robbinsdale Public Schools; Miss Helen Engelbretson, Social Worker, Robbinsdale Public Schools; Mr. Bill Moonen, School Psychologist, Robbinsdale Public Schools; Dr. Harold Ireton, Clinical Psychologist; Mrs. Mary Cordingley, Social Worker; Dr. Richard Chilgren, Pediatric Metabolic Resident; Dr. Paul Moe, Pediatric Neurologist and Dr. Robert ten Bensel, Moderator.

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M.M.

Child Psychiatry

The Child and the Physician*

Children epitomize the concept that tomorrow is today. We who work with children — and most of us do unless we are internists or geriatrists — have a share in molding that tomorrow. It is a challenging responsibility. In this — the first of the series — we will discuss some of the real differences between the practice of medicine with adults and with children. Perhaps because the differences are so simple, they are often overlooked.

Physician-Patient Relationship

In the practice of medicine with adults, the physician-patient relationship is usually on a one-to-one basis. True, the physician may include members of the family in his management of the patient, but essentially he deals directly with the patient. It is quite different in the case of a child. Here the physician invariably is dealing with a situation in which two or more individuals are involved. He tries to determine as quickly as possible what the pertinent factors in the complaint are. Usually it is the parent — not the child — who gives the complaint. The latter, particularly if he is an older child, should be encouraged more often to tell his own story. Three possibilities must be considered:

1. There may be something wrong with the *child*. Does he have an infection, a malignancy, or a deficiency of some type?
2. The parent may be bringing the child as an "admission ticket" when actually he wants help in understanding and managing the child. In other words, is the *parent* seeking counsel and guidance?
3. *Both* the parent and child may need assistance in resolving a stubborn, unhappy interpersonal relationship.

None of the three possibilities emerges in pure culture, because the parent-child relationship is so intimate. To illustrate, a child may require an operation. At the same time, parental concerns about the child's welfare must also be recognized and relieved. The physician's failure to do so can further complicate an already difficult situation. Similarly, though the parent may himself be seeking help, the child should be carefully examined. If a troublesome interpersonal relationship seems to be the main problem, recognition of the accompanying stress for both parties offers many opportunities for amelioration.

Patient Motivation

The adult comes to the physician for relief of his suffering. Central to it may be a physical disorder, an emotional problem, a feeling that he is a failure or that the difficulties of living are overwhelming. The adult manifests his confidence in the physician by *coming* to him. The child, on the other hand, is *brought* to the physician by a parent or parental surrogate.* The doctor may be the last person the child wishes to see;

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*In the hope of stimulating further interest in the art of dealing with children and their parents, the editor has agreed to publish a series of papers on subjects of special relevance.

*See Test Your Word Score Page 1167.

Continued

chances are his training, knowledge, skill, or erudition will 'cut little ice.' The child is interested in what kind of person he is. Does he like and understand children? Can he be trusted? No matter how gracious or smooth his professional demeanor may be, he cannot hide behind it. The child knows intuitively what he is.

The case of Daniel, aged six, illustrates this point. During the first visit the physician was most condescending in his speech and manner. Daniel tolerated the procedures until the time arrived for auscultation of the heart and chest. The physician, trying to ease his patient's discomfort, said soberly, "Now Danny, my little man, let me listen through this telephone." That was too much! "Doctor," Danny shot back, "some people call that a stethoscope." The physician suddenly realized he had better change his approach.

Communication

The physician uses different avenues of communication with children than with adults. Nonverbal systems predominate with the infant and the toddler. Plant states it this way: "Our rich and adequate contacts with young children are through the psychomotor tensions." Messages are carried by how we hold a child, turn him over, auscultate and percuss. Facial expression, eye movements, tone of voice, cadence, and timbre are important — particularly when the child is a little older; but too often we forget about these factors.

Most children begin to formulate sentences between the ages of 18 to 24 months. At five or six years the average youngster has a working vocabulary of several thousand words. By this time verbal communication supplements though never entirely supplants nonverbal communication. Words, however, do not always convey the intended meaning; they can be traps as well as useful tools, even between adults. The physician dealing with children must make doubly sure that the child actually understands what he says, and that he understands what the child tells him.

Attitude Toward Child's Problems

The problems of adults are taken seriously; at least, we give them a fair hearing. But too frequently we regard children as "little people with little problems." We need to remind ourselves that every human being is engaged in the struggle to master successfully the problems of his own everyday life, the fight to maintain a sense of dignity and balance. This is true whether the individual's age is one month or five years or 10 or 20 or 50 years. Actually, the child's struggle may be more intense than the adult's, because his dependency on others sometimes increases tensions to the point where his frustration tolerance is threatened. If we are to appreciate fully the child's need to maintain a sense of his own worth, we must accept the simple fact that he — like everyone else, regardless of age — has problems of life adjustment which can undermine his self-confidence and security, problems which look big to him.

Roles of Physician

The roles we assume as physicians dealing with children and their parents may be different from those we assume in dealing with adults.

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*See Test Your Word Score Page 1167.

For the child, we temporarily become a substitute parent; for the parents, we stand in the symbolic role of a parent. Fulfilling these roles and being mindful of their implications require each of us to examine our own attitudes, not only toward the children and parents, but toward ourselves and our procedures. The manner of our approach unquestionably reflects our basic orientation.

Parents usually are full of questions; we must be careful not to close the door on them. They expect us to counsel them in matters concerning their children's emotional and social development as well as in their eating, sleeping, and toilet training programs. Counseling, as distinguished from giving direct advice, means that we think a problem through *with* the parents, give them information, perhaps offer alternative courses of action for their consideration: in other words, that we help *them* make a decision rather than make it for them. This approach increases the chances for success because the parents presumably are ready to take the action agreed upon. If it fails, however, they tend to be more willing to try another tack instead of shrugging their shoulders and muttering, "The doctor doesn't know what he's talking about." This is not to say direct advice should never be given. Circumstances may demand it. But the manner in which it is given must be tailored to the circumstances and the individuals involved.

Preparation for Initial Visit

It is important for the physician dealing with children to ascertain what kind of preparation the child received before his first visit. A 12-year-old boy who was brought to a child psychiatrist is a case in point. It was unusually difficult to establish a friendly relationship with him. Every gesture the physician made was firmly and definitely rebuffed. Eventually the child became very restless. Noting the lad's increasing discomfiture, the psychiatrist said, "Something seems to be troubling you. Tell me about it." Hesitantly the child asked, "When are you going to look at my teeth? My mother told me I was coming to see a dentist." No wonder both doctor and child were floundering!

Direct

Direct preparation of the child by the parent is better now, on the whole, than it was years ago; however, there is no guarantee. Occasionally parents still use us doctors as a threat: "What will happen to you if I have to take you to the doctor?" they ask. This presents an unnecessary additional hurdle. If we are on the alert for opportunities, we can help parents do a better job.

Indirect

The indirect preparation a child receives may be even more unsettling and significant. Casual comments of parents or relatives about their own particular experiences with a physician; or, more maliciously, hair-raising tales of other children about their adventures with doctors and hospitals may get us off to a poor start. Phantasy is stimulated; questions are raised but not answered. The result may be an extremely anxious patient. In all probability our difficulties with some children are due in part to adverse

Continued

conditioning. An awareness of this possibility may help us win the confidence of the child. Once we have done that, is it not true that he will cooperate with us in the most trying, difficult procedures?

Reynold A. Jensen, M.D.
Minneapolis, Minnesota

Anglo-Saxon Leechdoms for Worms*

Against a hand worm, take ship tar, and sulphur, and pepper and white salt, mingle them together, smear therewith.

If a worm eat the hand: take marsh maregall, red nettle, red dock, and the small bur, boil in cows' butter; when the salve is sodden, then further take of salt three parts, shed thereupon, shake together and smear therewith; lather with soap, about night-time smear therewith.

Against a deaw worm (foot worm), let the man step upon a hot coal; let him cool (his foot) with water, let him step upon it, as hot as he hottest may.

For a deaw worm, some take warm thin ordure of man; they bind it on for the space of a night. Some take a swine's lung warm.

If the ana worm (bot) grow in a man smear with the black salve. If the worm eat through to the outside and make a hole, take a drop of honey, drop it on the hole, then have broken glass ready ground, shed it on the hole; then as soon as the worm tastes of this he will die. A salve against the ana worm thus shall one work; take cinquefoil, that is five leaf, and rue, boil them in butter, sweeten with honey.**

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*The generic term 'worm' probably included all very small marauders on man: worms, insects, pediculi, mites, fungi, etc.

**Payne, Joseph F., M.D. Oxon.: English Medicine in the Anglo-Saxon Times, Oxford at the Clarendon Press, 1904, p. 44-46.

Adoptive Parents Needed

Because of the increasing number and rate of illegitimate births, the number of children in need of adoptive homes has increased by geometric proportions in the past few years. For example, the Children's Home Society of Minnesota, 2230 Como Avenue, St. Paul, a state-wide nondenominational adoption agency, accepted and placed 100 children in 1953. In 1963, this Society placed 227 children and in 1964, 245 children; and still the agency can accept fewer than half the number of children referred to it.

Today the Children's Home Society of Minnesota, a United Fund agency, has one couple for every child in its care. However, with the ever-increasing number of children that are becoming available for adoption, it is necessary that the number of couples seeking children must also increase. Adoption procedures have gone through a great transformation since the Children's Home Society of Minnesota was organized in 1889, and therefore, the Society encourages couples and families to consider the adoption of a child or an additional child. The Society has no limit as to number of children placed with any one family. As long as there is reasonable financial security and ability to meet the basic needs of an additional family member, an application will be encouraged.

Grand Rounds

Dermatomyositis*

Dermatomyositis is a disease of multiform nature, usually associated with cutaneous lesions, extensive muscle weakness and muscle tenderness.

In 1887 Wagner described a 34-year-old female with painful muscles and joints and weakness of the shoulder girdle, who died a few weeks after she was first seen. This was one of the first clinical descriptions of acute dermatomyositis. Oppenheim was the first to emphasize the similarity of dermatomyositis and progressive scleroderma. In 1905 Steiner reported one of the first cases recognized in America.

Polymyositis hemorrhagica, dermatomucomyositis, neuromyositis, dermatoneuromyositis and angiomyositis are terms formerly used to designate dermatomyositis.

Incidence

Dermatomyositis has been found to be most frequent in the fourth and fifth decades of life with the age range between 20 and 69 years.[1,4,5] The disease was fatal in 40% of one group of cases. It is more common among females.[3]

Etiology and Pathogenesis

The etiology of the disease is not known. Bacteria, including streptococci and staphylococci, viruses and parasites have been implicated in an attempt to explain the pathogenesis. Wedgewood et al. measured the serum antistreptolysin titer in seven patients during the acute phase of the disease and found no elevation.

Hypersensitivity to toxins, drugs, especially the sulfonamide compounds and penicillin, sunlight and other agents have been suggested as causal.

Curtis and co-workers[1] reported that 7-15% of adult patients with dermatomyositis have associated carcinoma. In one series of 23 patients over 40 years of age, 12 (52.2%) had associated malignant disease[2] which may elaborate antigen to which the body responds with antibodies.[1]

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*Presented as a Medical Grand Rounds at Mt. Sinai Hospital, Minneapolis, February 23, 1965.

Continued

Immunoelectrophoretic studies have shown that in patients with dermatomyositis and lupus erythematosus, there is an increase in the alpha beta and gamma globulins. Also identified in dermatomyositis and scleroderma are gamma globulins which react with cell nuclei. Antinuclear fluorescence has been found in patients with rheumatoid arthritis, scleroderma and dermatomyositis.

Pathology

O'Leary and Waisman reported that the initial pathologic reaction involves plasma cells, histiocytes, fibroblasts and mast cells. Precapillary arterioles and venules may show thickening of their walls. Collagen deposits, localized areas of necrosis, cellular infiltration and increased vascularity extend into the subcutaneous spaces. Whether the subcutaneous tissue is affected by direct extension from the skin peripherally, or the muscles centrally, has not been determined.

The heart muscle may show swelling and early pyknosis of the nuclei of individual fibers. In isolated instances, nonbacterial endocarditis and pericarditis have been observed.

Ulcers of the esophagus, stomach, portions of the small bowel and rectum have been described. The ulcerations have been associated with edema and cellular infiltration of the walls of the arteries and veins. Subsequent stages of this process lead to mucoid and fibrous thickening of the intima, with narrowing of the lumen and thrombosis.

The kidney is particularly susceptible to extensive vascular changes. One patient with dermatomyositis seen early during the course of her disease developed generalized calcinosis with skin changes that suggested scleroderma. Pathologic examination of the kidneys showed endarteritis of the interlobular arteries.

Wedgewood et al. consider the vascular lesions in dermatomyositis more difficult to distinguish from those of thrombotic thrombocytopenic purpura but unlike those of polyarteritis, in that necrosis and inflammation of the vessel wall are minimal or absent.

Clinical Findings

The disease may begin insidiously with a low-grade fever, malaise, minimal aches and pains of the extremities, and without any significant antecedent illness. Twenty-four per cent (24%) of cases reported by Sheard had sudden onset; 32% complained of edema or a rash on the face as a presenting symptom.

Cutaneous Manifestations

Some patients may suffer an acute viral or bacterial infection at the onset of the illness; cutaneous manifestations in some patients precede symptoms of muscle involvement.

Erythema may be present with or without subcutaneous edema and may be mottled or diffuse, livid or rosy. The term "heliotrope" has been applied to the appearance of the affected eyelids. The face and the anterior neck are common sites of the erythema, followed in frequency by involvement of the extensor surfaces of the arms, the legs and the trunk. When edema is present, it may be pitting, brawny or indurated. Purpura, vesicles and bullous formation have been reported.

During the natural course of the disease, the cutaneous manifestations undergo alteration; pigmentation, atrophy and telangiectasia may predominate at a later stage. These changes may be sharply demarcated from normal skin on the exposed portions of the body. The similarity to the dermatitis of pellagra, the pigmentation of adrenal insufficiency or localized morphea may confuse the presumptive clinical diagnosis. Wedgewood noted erythematous, atrophic and scaly lesions in children, with a network of fine blood vessels visible over the extensor surfaces of the joints, particularly the knuckles, elbows and knees. Partial alopecia has been reported in several patients.

Muscular Manifestations

Muscular weakness, aching and fatigue may be a prominent or an insignificant clinical feature. Any striated muscle may be affected, although there is a tendency for the development of bilaterally symmetric lesions. The large muscle masses are more likely to be involved than the pharyngeal, laryngeal, intercostal, diaphragmatic or ocular groups. The proximal muscle groups of the upper and lower extremities are more likely to be involved than the distal goups.

A majority of patients have diffuse muscle tenderness. Extensive involvement upon microscopic examination has been found in muscles that have been neither painful nor tender on palpation. The consistency of involved muscles may be normal, doughy, firm or fibrous. Weakness of facial and glossal muscles makes eating and speaking difficult. Extensive involvement of the muscles of respiration and deglutition may occur. Muscle atrophy is common, and extensive fibrosis with contractures of the elbows, knees, hips and fingers develops if the disease progresses to a subacute and chronic phase.

Ocular Changes

Lisman has described in detail the ocular changes in one patient with dermatomyositis and compared his findings with a similar case reported by Bruce. The patient, a 53-year-old male, had suffered generalized weakness for approximately six months. His eyelids were swollen and the surrounding skin was pink from telangiectasia. The edematous area of infiltration pitted upon pressure. The lower lids hung in folds and were tender to touch, attributed to involvement of the orbicularis oculi. Post-mortem examination showed hyaline and lipid changes in the external plexiform layer of the eye, especially around the macula, and a few scattered hemorrhages in the retina. The vessels showed no pathologic changes.

Other Changes

The bronchi and lungs may be involved and symptoms of cardiac dysfunction have also been observed.

Involvement of the gastrointestinal tract may produce symptoms that are indistinguishable from those of systemic scleroderma. These include stomatitis, myositis of the tongue, dysphagia and epigastric distress. Splenomegaly and lymphadenopathy may be present.

Central and peripheral nervous systems may be affected, with resulting confusion, psychosis, delirium, diminished tendon reflexes, hyperesthesia, numbness of the hands and feet, and foot drop.

Continued

The association of dermatomyositis with myasthenia gravis or with thyrotoxic myopathy has been discussed by Ragan and Dawling. The muscle weakness of myasthenia gravis or severe thyrotoxicosis bears a casual similarity to that of dermatomyositis. Microscopic examination of the affected muscles reveals selected pathologic changes common to each illness.

Diagnosis

The disease may be suspected in patients with atypical rheumatoid arthritis or with acute rheumatic fever, who do not respond to therapy. Muscle weakness or tenderness, particularly of the shoulder girdle and upper arms, together with skin lesions, fever and malaise, should suggest the possibility of acute dermatomyositis. Inquiry should be made regarding a previous history of Raynaud's syndrome or of presenting complaints of facial or periorbital edema. Pathologic changes in muscle and skin lesions from biopsy material are helpful in diagnosing the mild or early case. However, a negative biopsy in a patient with clinical evidence of dermatomyositis does not exclude the diagnosis. The severity of the myositis is related to the clinical severity of the illness. Early in the course of the disease it may be difficult to distinguish this disorder from the edematous stage of scleroderma* or scleredema.

Clinical Course

In most instances the disease is considered fatal. The clinical findings usually become progressively worse. More than 50% of the patients with the acute fulminating type die without a demonstrable remission. Death within eight weeks from the onset of symptoms has been reported. The average expectancy under current therapy in patients without a malignant tumor is approximately three years from the onset of clinical symptoms. Survival may be prolonged for a decade or more if the disease becomes partially quiescent and regresses into the subacute or chronic stage. Remissions with apparent restoration of health have been observed to occur spontaneously, induced by steroid therapy and following removal of an associated malignant tumor. Death from intercurrent infection, cardiac failure or renal insufficinecy may be expected in the acute fulminating type.

The series of Talbott et al., recently brought up-to-date, shows only two patients alive and in remission. One, a 51-year-old female, has experienced a remission for more than 18 months, thought to be associated with adrenal steroid therapy.

Cause of death before the antibiotic era was due to overwhelming infection. Cardiac failure from myocarditis may lead to death, as may pulmonary insufficiency caused by progressive fibrosis.

Laboratory Findings

Blood studies may show an elevated white count with a relative lymphopenia and polymorphonucleosis and occasionally an eosinophilia as high as 25%. Sedimentation rate may be elevated out of proportion to the constitutional symptoms.

During the active stages of muscular weakness transaminase is released from damaged skeletal muscle fibers into the peripheral blood; its determination provides a valuable clue as to the continued progression of muscle necrosis. As recovery begins, the enzyme levels return to normal.

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*See Test Your Word Score Page 1167.

In eight cases reported by Pearson, seven had elevated levels of serum glutamic oxaloacetic transaminase. The lupus erythematosus clot test is negative. Slight increase in gamma globulin has been observed. There has been no characteristic alteration in the electrolyte pattern.

An electrocardiogram may show changes suggestive of interstitial fibrosis of the myocardium. The alteration consists of prolongation of P-R, QRS and Q-T intervals, minimal variations in the appearance of RS-T segments and T waves, as well as slurring and notching of QRS deflections in multiple leads.

X-ray Findings

When dysphagia is a complaint, roentgenographic study of the swallowing mechanism may reveal weakness of the pharyngeal musculature and pooling of barium in the pyriform sinuses and valleculae.* Fluoroscopic examination of the chest may show diminished expansion of the lungs and reduced excursion of the diaphragm. X-ray study may reveal interstitial infiltration or diffuse fibrosis. Examination of the soft tissues in chronic cases may show extensive subcutaneous calcification and osteoporosis. Calcium deposits occur along fascial planes such as in the axillae and the plantar surfaces of the feet, as well as in the subcutaneous areas along the extensor surfaces of the forearms and in the subcutaneous spaces of the fingers, toes and buttocks.

Electromyogram

Electromyography reveals action potentials of short duration which may be polyphasic and reduced in size, with little or no reduction in the total number of motor unit discharges on voluntary contraction. Spontaneous fibrillations are recorded in the active phase.

Treatment

Until the advent of steroid therapy the treatment of dermatomyositis had been ineffective.

Steroids suppress the inflammatory reaction in the muscles, and with adequate dosage the patient becomes more comfortable, complications are reduced, and the extent of residual crippling is lessened considerably. Few patients, especially children, escape without residual disability. The possibility of relapse must always be anticipated. The length of time steroids should be continued has not been established. Treatment courses lasting for six to 18 months are not unusual.

Antimalarial drugs and anabolic agents such as testosterone or norethandrolone have been tried, but benefit is questionable.

Supportive therapy should include prophylaxis against intercurrent infections. These patients are particularly vulnerable to respiratory infections. Contracture cannot be avoided, but it can be kept to a minimum by heat and splinting. Physical therapy to keep the joints and muscles supple may be introduced after the acute phase subsides. Activity should be restricted.

Case Summary

A 14-year-old white female had appearance of edema of the eyelids in March, 1964. There had been no preceding febrile illness, allergy, medication or dietary indiscretion.

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*See Test Your Word Score Page 1167.

Continued

At the start there was some improvement of the lid swelling with antihistamine; but soon the swelling became fixed and so marked that it interfered with her vision. She was first hospitalized in May, 1964, and treated with prednisolone. About two weeks prior to that hospital admission she had developed muscle aching and soreness, mostly in the upper arms, shoulder girdles and lower back. There was no disturbance in gait, tremor or fasciculation noted.

In November, 1964, she developed pain in the left neck with diffuse hard swelling which gradually subsided. She was able to continue her schooling and to participate in the farm work and household chores despite awareness of increasing fatigability and progressing weakness on exertion. Family history and system review were negative.

On November 20, 1964, she was admitted to Mount Sinai Hospital for the first time.

Physical examination on admission revealed a well developed, well nourished female. The most striking finding was the presence of tense edema of the eyelids with a purplish-reddish hue. Near the inner canthus of the right eye the skin was shiny. There were no conjunctival abnormalities. The remainder of the examination was entirely negative except for a noticeable weakness of the sternocleidomastoid muscles and also the muscles of the shoulder girdle, particularly on the left. Neurological examination showed a generalized hyporeflexia of the deep tendon reflexes bilaterally. Cranial nerves were normal.

Laboratory Findings

Laboratory examination revealed the following. Urinalysis showed specific gravity of 1.020, pH 6, 50-70 rbc and 5-8 wbc. Hemoglobin was 13.3 gm% and hematocrit 43%. White blood count was 5,100 with 53% neutrophiles, 38% lymphocytes and 9% eosinophiles. Serum chlorides 105 meq/L, Na 141 meq/L, potassium 4.5 meq/L, calcium 9.1 mg%. Platelet count 230,000. Bleeding time 3.3 min. Prothrombin time 12.9 sec. Phosphorous 5.8 mg%. Venereal disease research laboratory test for syphilis negative. Blood urea nitrogen 21 mg%. Sedimentation rate 28 mm. in 1 hour. Serum transaminase was 178 and 140. Uric acid was 6.8 mg%.

Muscle biopsy revealed moderately extensive degenerative changes in the skeletal muscle fibers with vacuolization and hemogenization of sarcoplasm. Scattered myofibers were fragmented and hyalinized and appeared to show partial phagocytosis. Occasional small muscle groups were largely atrophic and showed partial replacement by fibrous tissue. The changes were consistent with those occurring in progressive dermatomyositis. Electromyographic studies revealed myopathy involving the proximal muscle most severely.

Treatment and Course

In May, 1964, she was first treated with adrenal cortical steroids and kept at bed rest. During the summer months her muscle pain subsided, but she began to have progressive weakness of the muscles of the left shoulder and biceps. There was a noticeable change in the quality of her voice which became more nasal. She also had regurgitation and difficulty in swallowing liquids. Her diet was somewhat limited, but no marked weight loss occurred. The steroid dosage was gradually reduced, and by late July, 1964, she was able to resume partial activity. A program of physical rehabilitation was begun. In August, 1964, she was considerably stronger and the steroids were discontinued. She was allowed to go back to school, but in October, 1964, renewed activity appeared with facial erythema and edema and aching of the muscles of the shoulders, neck and back.

Prednisolone therapy was again started and, in addition, sodium salicylate was given. On admission to Mount Sinai because of progression of symptoms the prednisolone dosage was increased to 48 mg. per day. Besides prednisolone she was also receiving 90 grains of aspirin daily.

In January, 1965, her case was presented to the University Dermatology Conference, and it was suggested that high dosage of steroids be continued. Despite this therapy her muscle pain and weakness became progressively worse, and she began to have persistent regurgitation of liquids through the nose and contractures of the left arm and right leg.

On February 18, 1965, she was transferred to the University of Minnesota Hospital.

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Advances

Antidepressant Drugs

Review and Application*

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ENCOURAGING A depressed patient to swallow something is not a recent innovation. Alcohol has been used for thousands of years to alleviate the melancholy moment. Opiates and barbiturates, and more recently, amphetamines, have been used in depressive illnesses; but only within the last decade have antidepressant agents without intoxicating and habit-forming properties been available. These newer substances are both touted as panaceas for the miserable and disparaged as the profitable promotions of their manufacturers. Such debates are not new in medicine, and only time will prove whether these agents are really valuable. Nevertheless, these drugs are in wide use, and their careful consideration is warranted.

Depression is hard to define, to describe, and to classify. The term may designate a *symptom* when used to describe a feeling state associated with many illnesses and situations; or it may designate a *syndrome* (a collection of symptoms) such as neurotic depressive reaction. Rarely has it been used to mean *disease*, such as manic-depressive disease, which would imply a specific etiology.[1] In general, drugs used in psychiatry are symptomatic (nonetiological) therapies. Simple sadness or crying is not usually an indication for an antidepressant drug. One difficulty in assessing the literature of these therapies is the difficulty in determining what was treated — symptom or syndrome? As a symptom, depression is common to all men, but it is also extremely transient and likely to abate spontaneously. As a syndrome, depression is also common, and while both spontaneous and placebo remission rates are high, therapy can be crucial. Further complicating the assessment of antidepressant drugs is the availability of a proven therapy, electroshock. Some controlled evaluations of antidepressants have used for subjects patients with poor prognoses who may not have responded to electroshock or other therapies. All told, the problems posed by indications, spontaneous remission, placebo response, availability of electroshock, and the kinds of subjects used in some studies have resulted in a mass of contradictory reports.[2]

Why, then, use drugs? The reasons are few and simple. First, drugs can be used by all physicians. Second, antidepressant agents do not interfere with daily functioning, and patients, if helped, prefer them to electroshock.[3] Finally, desire for a prescription can bring a patient to the physician's office for necessary psychological support and direction. Patients generally expect tangible treatments, and the popularity of antidepressant drugs depends, in part, on this

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expectation. Fulfilling the expectation need not be defended, but it should not be encouraged. Despite their limitations, antidepressant agents used judiciously and knowledgeably with other medical treatments can prevent many disasters.

Psychiatric Drugs

Benson and Schiele[4] have classified psychotropic drugs as major tranquilizers, minor tranquilizers, and antidepressants; Table 1 is an adaptation of their classification. Drugs used in depressions can be classified on the basis of pharmacodynamic activity.

Central Nervous System Direct Stimulants — the Amphetamines

Although they provide immediate euphoriant effects, the amphetamines are minimally useful in treating classic depressive syndromes; however, rapid development of tolerance and the danger of habituation or general abuse limit their use. They sometimes help counteract sedation induced by anticonvulsants and other sedatives and, on occasion, are helpful in grief reactions; but they are contraindicated in alcoholism or any addiction, and in the triad of passivity, obesity, and fatigue common to certain depressive conditions. Table 1 lists the two most potent and habit-forming amphetamines first and the three least potent and habit-forming last.

Indirect Stimulants — the Monoamine-Oxidase Inhibitors

TABLE 1

Drugs Used in Depressive Syndromes

- A. Central Nervous System Stimulants
  - 1. Predominantly Direct Stimulants
    - a. Amphetamine (Benzedrine)
    - b. Dextroamphetamine (Dexedrine) (Biphetamine)
    - c. Methamphetamine (Desoxyn) (Ambar Tablets)
    - d. Pipradrol (Meratran)
    - e. Methylphenidate (Ritalin)
  - 2. Indirect Stimulants
    - a. Isocarboxazid (Marplan)
    - b. Phenelzine (Nardil)
    - c. Nialamide (Niamid)
    - d. Pargyline (Eutonyl)
  - 3. Bimodal Stimulants
    - a. Tranylcypromine (Parnate)
- B. Central Nervous System Suppressants
  - 1. Imipramine (Tofranil)
  - 2. Amitriptyline (Elavil)
  - 3. Desipramine (Pertofrane) (Norpramin)
  - 4. Nortriptyline (Aventyl)
- C. Miscellaneous Agents
  - 1. Various of the minor tranquilizers — Valium, Equanil, Librium, Vistaril, etc.
  - 2. Benactyzine (Suavitil), deanol (Deaner), benactyzine and meprobamate (Deprol)
  - 3. Various of the phenothiazines — Stelazine, Mellaril, Thorazine, etc.

In 1952 two hydrazine derivatives of isonicotinic acid, isonazid and iproniazid, were introduced in the treatment of tuberculosis. A number of individuals receiving these agents experienced elevation in mood.[5] Iproniazid, in particular, seemed to be a potent inhibitor of monoamine oxidase, an enzyme which facilitates the degradation of epinephrine, norepinephrine, and serotonin. Encouraged by the mood changes observed in tuberculous patients receiving iproniazid, investigators studied the effects of other monoamine-oxidase inhibitors in psychiatric patients. Initial reports were encouraging, with beneficial results reported in 50 to 80 per cent of depressed and schizophrenic patients,[6,7] many of whom had not responded to phenothiazines or electroshock. However, later studies have been generally less enthusiastic, although some have reported good responses in certain depressed patients.

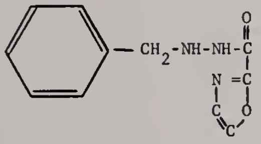
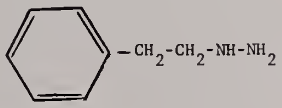
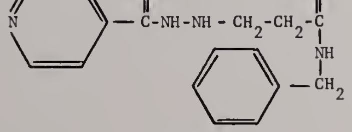
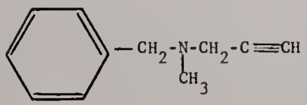
Pharmacologic Action

In vivo examinations show that administration of monoamine-oxidase inhibitors of the hydrazine type results in the presence of increased amounts of the endogenous monoamines in various organs. This increase persists for several days and therapeutic doses have a cumulative effect. Besides elevating the monoamines in the brain, these agents increase the norepinephrine and epinephrine levels in the heart and the lactic and pyruvic-acid levels in the peripheral blood. An interesting clinical effect exploited in the treatment of hypertension is that these agents are also ganglion blockers, and large doses inhibit transmission through the sympathetic ganglia without equally depressing the function of parasympathetic ganglia. Hydrazine-type monoamine-oxidase inhibitors also influence a number of other enzyme systems; but species differences make elucidation of specific effects in man doubtful.[8] Table 2 illustrates the chemical formulae of the available compounds.

Not fully understood is the mechanism responsible for the principal *clinical effect* of the monoamine-oxidase inhibitors (psychostimulation, pain relief, alleviation of angina pectoris, and hypotension). Investigating the role of monoamine-oxidase inhibition is complicated by the variable potency of these agents from species to species. Consequently one can make only partial deductions about the quantitative action of monoamine-oxidase inhibition in man on the basis of animal experiments. Also, changes in the content of the amines and their metabolites in human urine do not necessarily reflect corresponding metabolic changes in the brain or myocardium. The organs contain a small fraction of the amines; the larger fraction is localized in peripheral depots (the adrenal medulla, etc.). However, the clinical effects of these drugs seem better correlated with monoamine-oxidase inhibition and changes of monoamine metabolism than with inhibition of any other enzyme system investigated to date. Of interest to nonpsychiatric clinicians is the apparent influence of monoamine-oxidase inhibitors on mesenchymal inflammation and connective-tissue growth.[9] Also, chronic-pain syndromes sometimes diminish or disappear, suggesting that these agents increase the threshold to certain types of pain.[11] Moreover, indolent ulcerations and certain burns have benefited from topical treatment with hydrazine monoamine-oxidase inhibitors.[10,12]

Early clinical effects include central nervous system stimulation, which may be manifested by mood elevation; in some instances

TABLE 2
Indirect Stimulants
(Monoamine-Oxidase Inhibitors)

Structure	Generic Name	Trade Name
	Isocarboxazid	Marplan
	Phenelzine	Nardil
	Nialamide	Niamid
	Pargyline	Eutonyl

Continued

this may be paradoxically characterized by drowsiness or generalized relaxation. In certain patients no apparent effect on psychomotor state is observed. An effect on the autonomic nervous system occurs consistently, usually coincidentally with other physiological effects. Occasionally the effect of sympathetic or parasympathetic activity occurs before the mood change. This effect varies in severity and location in different individuals.

The Indications for Treatment

Illness generally treated with monoamine-oxidase inhibiting agents includes depression, especially prolonged depression with psychomotor retardation. The indirect stimulants are also useful in certain chronic neuroses and psychoses of other types. In addition, reports suggest these drugs to be beneficial in angina pectoris;[13] but whether they offer more than symptomatic pain relief due to analgesia and psychomotor stimulation is not clear. Like most subjective complaints, angina pectoris appears to be benefited considerably by the hydrazines in uncontrolled clinical trials, but when assessed with a placebo, benefit is difficult to prove.[14] When one considers the possible dangers of orthostatic hypotension or psychologically induced pain reduction, it seems sensible to use these agents conservatively in angina pectoris. The hydrazines and a nonhydrazine compound (pargyline) have also been used to treat hypertension.[15,16]

Since these agents cause widespread multiple effects in various systems of the body, *side effects* are somewhat difficult to define. The following are generally reported: vascular headaches, flushing, perspiration, lightheadedness, vertigo, postural hypotension, nausea, constipation, tremors, anorexia, increased appetite, urinary hesitancy, alteration in sexual activity, muscle fasciculations,* hyper-reflexia, clonus, edema, dry mouth, and paradoxical excitement. Serious toxic effects include necrosis of the liver, anemia, leukopenia, acute confusional and functional psychoses, and cardiac arrhythmias. Fever, hypertension and seizures sometimes occur when these agents are combined with imipramine, amitriptyline, desipramine, and nortriptyline.

There have been recent reports of catastrophic vascular reactions to the monoamine-oxidase inhibitors, and paroxysmal hypertension with severe headaches has resulted from their conjoint administration with sympathomimetic agents. Since 1963, a number of vascular crises have occurred after individuals taking these agents have ingested cheese, beer, broadbeans, etc., all of which contain large amounts of tyramine, whose potentiation may have been responsible.[17] In one large study of vascular disasters, approximately 8.4 per cent of patients receiving monoamine-oxidase inhibitors experienced acute hypertensive crises featuring intense occipital headaches and palpitation.[18] When patients are warned about ingesting cheese, processed milk products, and certain alcoholic beverages, the incidence of hypertensive crisis falls considerably. The biggest offender in this group of drugs has been tranylcypromine; but other monoamine-oxidase inhibitors are also likely offenders.

The hydrazine monoamine-oxidase inhibitors potentiate the pharmacological action of numerous unrelated drugs, including ganglion-blocking agents, barbiturates, anesthetics, corticosteroids, morphine, atropine, 4-amino-quinoline compounds, and alcohol. It is interesting to note that the diuretics, chlorothiazide and hydrochlorothiazide, potentiate the hypotensive effect of the hydrazines.

Assessment of Efficacy

At present, three indirect stimulants are available, namely, the hydrazines *isocarboxazid* (Marplan), *phenelzine* (Nardil), and *nialamide* (Niamid). The nonhydrazine *pargyline* (Eutonyl) was recently introduced as an antihypertensive agent. All have been assessed with and without placebo controls. Many uncontrolled investigations suggest that these agents are effective in many types of depression, especially in chronic, long-term depressions with somatic complaints and psychomotor retardation. The relatively rare, controlled investigations suggest the following: (1) Two large studies found isocarboxazid inferior to imipramine and placebo,[19,20] but three others found it more effective than placebo.[21-23] (2) Nialamide was also found ineffective in three controlled studies,[24-26] but according to another was superior to placebo.[27] (3) Four studies found phenelzine, like the others, inferior to electroshock.[20,28-30] Some controlled studies of phenelzine indicate it is superior to placebo,[31,32] but others indicate it is not.[20,28] (4) One controlled investigation found pargyline inferior to tranylcypromine.[33]

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*See Test Your Word Score Page 1167.

Tabulation of Specific Agents

Isocarboxazid (Marplan) — Its manufacturer and reports in the literature suggest that isocarboxazid is useful in various psychiatric disorders associated with depressive symptoms, withdrawal, or regression. It is provided in 10 mgm. tablets, and the usual starting dosage is 30 mgm. daily. Since its action is cumulative, dosage should be reduced to 10 or 20 mgm. a day after a week, or when the drug begins to have effect.

Nialamide (Niamid) — Indications are similar to those for isocarboxazid. It is provided in 25 mgm. tablets, and the suggested starting dosage is 75 to 100 mgm. daily in either divided or once-daily doses. Dosage should be increased gradually to 200 mgm. a day. After two or three weeks, or when a therapeutic effect is attained, one should gradually reduce the dosage to about 75 to 100 mgm. a day.

Phenelzine (Nardil) — Indications are similar to those for other members of the group. Phenelzine is provided in 15 mgm. tablets, and the suggested initial dosage is 45 to 75 mgm. daily, with a maintenance dosage of 15 to 30 mgm. a day being achieved after several weeks.

Pargyline (Eutonyl) — As a *nonhydrazine,* pargyline should not cause an appreciable incidence of liver dysfunction, although this is by no means certain. While suggested for use primarily as an antihypertensive, this agent does possess some antidepressant qualities; however, at present it is not suggested for use as an antidepressant.

Central Nervous System Bimodal Stimulants (Tranylcypromine)

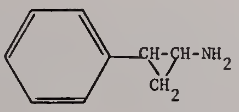
General

Currently the only bimodal stimulant available is tranylcypromine (Parnate). This was the first of its group, and subsequent compounds have proved either ineffective or too hazardous for clinical use. Although in vivo it is one of the most potent monoamine-oxidase inhibitors, it differs from the hydrazine inhibitors in several ways, including the low incidence of liver and blood disorders associated with its use. Also, its cumulative effect is slight and dosage regulation is thus not so difficult. Finally, side effects like constipation, tremors, and sweating are less frequent. These benefits are, however, counterbalanced by the severe vascular catastrophes reported in 1963. For a time the drug was not marketed, and it has only recently been reintroduced. Table 3 gives the formula for tranylcypromine.

Pharmacology

An arylcycloalkylamine derivative somewhat similar in structure to the amphetamines, tranylcypromine is one of the most potent in vivo monoamine-oxidase inhibitors as measured by various pharmacological tests. Like the indirect hydrazine and nonhydrazine stimulants, it has monoamine-oxidase inhibiting properties; but it also has effects like those of the amphetamines, including a pharmacological antagonism to

TABLE 3
Bimodal Stimulants

Structure	Generic Name	Trade Name
	Tranylcypromine	Parnate

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reserpine.[34] It will probably prove to have ganglion-blocking properties as well, since its side-effect pattern is in some ways similar to that of the other indirect inhibitors.

Indications and Assessment of Efficacy

Tranylcypromine has been used in the following clinical conditions: (1) neurotic depressions,[35,36] (2) retarded depressions[37] or (in conjunction with a phenothiazine) agitated, depressed syndromes,[38] (3) the withdrawn anergic, apathetic, chronic, hospitalized schizophrenic syndrome,[39] and (4) the multisymptom complex of somatic concern, anxiety, depression, and pseudoneurotic schizophrenia.[40] Controlled studies have indicated tranylcypromine is superior to placebo or reference compounds[41-43] but inferior to electroshock.[44] One recent investigation found that in combination with trifluoperazine it was superior to electroshock.[45]

Since the reports of vascular crises with tranylcypromine, the indications have been amended, and it is now indicated for severe depression in patients for whom electroshock is contraindicated or for whom no other drugs have been satisfactory. Also, tranylcypromine should be reserved for patients who are either hospitalized or under close supervision.

Side Effects

Side effects commonly associated with tranylcypromine are orthostatic hypotension, overstimulation, insomnia, weakness, headache, and palpitation. Rarer are drowsiness, dizziness, dry mouth, tremors, nausea, diarrhea, abdominal pain, bad taste in the mouth, and constipation. Anorexia, edema, blurred vision, chills, impotence, hepatitis and skin rash have been reported. Also rare are tinitis, muscle spasm, seizures, urinary retention, glaucoma, ventricular arrhythmias, and pulmonary edema.

Hypertensive crisis, the most serious reaction associated with the use of tranylcypromine, is characterized by some or all of the following symptoms: occipital headache which may radiate frontally, palpitations, stiff or sore neck, nausea or vomiting, sweating (sometimes with fever and sometimes with cold, clammy skin), photophobia, and dilated pupils. Either tachycardia or bradycardia may be present, possibly associated with constricting chest pains. Sometimes fatal intracranial bleeding has occurred.[46] In all patients taking the drug, blood pressure should be followed closely for evidence of any pressor response. One should not rely solely on blood pressure readings but also on frequent observations of the patient. Therapy should be discontinued immediately if palpitation or frequent headaches occur, as these may portend an incipient hypertensive crisis. If such a crisis occurs, the drug should be discontinued and therapy immediately introduced to lower blood pressure. Either pentolinium or phenotolamine is recommended.[47]

The contraindications specifically listed by the manufacturer are:[48] (1) Tranylcypromine is contraindicated in patients more than 60 years old, patients with confirmed or suspected cerebrovascular defects, and patients with cerebrovascular disease, hypertension, or history of headache. (2) It should not be given conjointly with imipramine, amitriptyline, desipramine, nortriptyline, pargyline, nialamide, phenelzine, or isocarboxazid; if any one of these drugs is given after tranylcypromine is discontinued, or if tranylcypromine is initiated after one of these drugs is terminated, the patient should be drug-free for one week. The drug should not be administered conjointly with any sympathomimetic agent, including the amphetamines and over-the-counter drugs such as cold, hayfever, or reducing preparations containing vasoconstrictors. (3) Patients should be instructed not to ingest cheese, broadbeans, processed milk products, beer, ales, and wine while taking the drug. (4) Also to be avoided are the antihistamines.

Tabulation of Specific Agents

The only agent in this group is tranylcypromine, which is provided in 10 mgm. tablets. Recommended initial dosage is 10 mgm. once or twice a day. After a week (provided no serious side effects occur), this dosage may be increased to a maximal daily dosage of 30 mgm. A suitable maintenance dose is 10 mgm. once or twice daily.

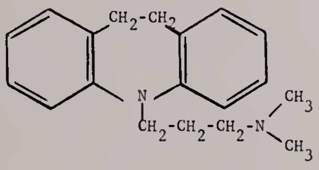
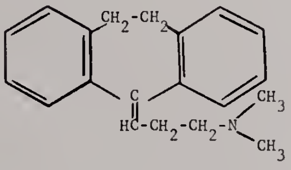
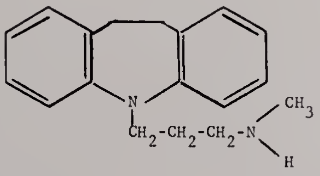
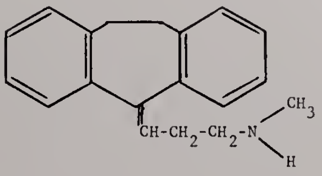
Central Nervous System Suppressants

Kuhn reported (1957) that an iminodibenzl derivative, imipramine, had antidepressant properties.[49] Since the monoamine-oxidase inhibitors were already clinically useful antidepressants, it seemed probable that this compound would have similar action. However, investigators found that imipramine and related compounds discovered at about the same time had many properties in common with the phenothiazines. Extensive clinical evaluations have demonstrated their value in many minor and severe depressive disorders, and they have, in general, proved beneficial in the agitated, depressive syndromes, especially in those of the involutional period. Side effects have consistently proven troublesome with adequate dosages. Table 4 illustrates the formulae for this group.

Pharmacology

All these agents exhibit weak to moderate activity similar to that of the phenothiazines. They impair the conditioned avoidance response, and other pharmacodynamic activities suggest similarity to the phenothiazines. Differences between the action of imipramine and the phenothiazines include the following: imipramine alerts the electroencephalogram; the phenothiazines sedate it. Imipramine and related agents potentiate the action of catecholamines, and all are antagonistic to reser-

TABLE 4
Central Nervous System Suppressants

Structure	Generic Name	Trade Name
	Imipramine	Tofranil
	Amitryptyline	Elavil
	Desipramine	Norpramin Pertofrane
	Nortriptyline	Aventyl

Continued

pine. In addition, amphetamine-induced psychomotor stimulation is slightly potentiated by subcutaneously administered imipramine, and imipramine and desipramine potentiate the effect of methyl phenidate, a central adrenergic agent, while chlorpromazine antagonizes it. In summation, the complex pharmacodynamic effect of these agents makes it difficult to assume a simple mechanism of action; the data imply, however, that they have anticholinergic, adrenosensitizing, and central nervous system stimulant properties.[4,50,51]

Indications

Although central nervous system suppressants are newer than the monoamine-oxidase inhibiting agents, they are in wider use, and it may be assumed that they are more acceptable to physicians. In uncontrolled studies, depressive states of diverse psychopathology have responded to imipramine, and claims of efficacy in the endogenous depressions have been particularly strong especially in manic-depressive reactions of the depressed type and involutional melancholia). The oldest of the three drugs are imipramine and amitriptyline, and both have delayed onsets of action; thus, an adequate trial requires two to three weeks.

Side Effects

Side effects of central nervous system suppressants include dry mouth, tachycardia, constipation, blurred vision, sweating, dizziness, weight gain, urinary frequency or retention, nausea, vomiting, orthostatic hypotension, and Parkinsonian tremors. Seizures, hypermanic episodes, myocardial infarction, fainting, skin rashes, and photosensitivity have also been reported. Hepatitis and bone-marrow depression, including agranulocytosis, are uncommon. Concomitant or temporally close administration of any monoamine-oxidase inhibitor should be avoided.

Assessment of Efficacy

Some controlled investigations on depressed patients have found imipramine significantly superior to placebo,[19,52,53] while others have not.[20,54] Controlled studies comparing imipramine to electroshock suggest equal efficacy at best[55] and inferiority at worst.[20] Imipramine has been found somewhat less effective than amitriptyline,[56] and both more effective[19,20,57] and less effective[21] than the monoamine-oxidase-inhibiting antidepressants phenelzine and isocarboxazid respectively. A study comparing it to tranylcypromine found the two comparable.[58]

Amitriptyline has also been found more effective than placebo.[59] Desipramine (Norpramin) has been reported to have a profile of activity similar to amitriptyline and imipramine;[60,61] controlled studies suggest it is superior to placebo[62] and comparable to imipramine.[63] Nortriptyline, another recently introduced central nervous system suppressant, is similar to other members of the group in indications,[64] and controlled studies suggest it is equal in efficacy.[65]

Individual Agents

Imipramine (Tofranil) — This drug may be given in a wide variety of depressive syndromes. It is supplied in 10 and 25 mgm. tablets and also in parenteral solution. Initial dosage should be from 25 to 75 mgm. a day, with a maximal daily dosage of 300 mgm. which should be given only under *very* close supervision. The average daily dosage is approximately 150 mgm. Dosage may be increased by 25 to 50 mgm. every few days, depending on toleration. The physician should exercise extreme care in administering imipramine to elderly patients because of the danger of orthostatic hypotension and cardiac arrhythmias. The claim that imipramine is effective in the treatment of enuresis[67] has been disputed.[68]

Amitriptyline (Elavil) — Greatly similar to imipramine, except that it is probably more sedative, amitriptyline is provided in 10 and 25 mgm. tablets. Suggested initial dosage is 75 mgm. daily, with a maximal daily dosage of 200 mgm. Dosage may be increased from 25 to 50 mgm. every three or four days. Contraindications and precautions are similar to those for imipramine.

Desipramine (Norpramin, Pertofrane) — This drug has an alleged rapid onset of action and was suggested for clinical use since it is a pharmacologically active metabolic product of imipramine. Twenty-five mgm. tablets are provided, and suggested initial dosage is 75 to 100 mgm. daily, followed by a week's rapid increment of up to 200 mgm. daily in divided doses. Side effects reported to date are similar to those for the group. Rarely, transient ataxia is seen, and a number of patients have reported a peculiar flushed, warm sensation of the skin.

Nortriptyline (Aventyl) — A recently introduced central nervous system suppressant with indications and possible adverse consequences similar to those for other members of the group, nortriptyline appears closer to amitriptyline than to imipramine on the basis of chemical structure. Capsules of 10 and 25 mgm. are provided. Recommended dosage is 20 mgm. daily initially, with subsequent increments to 100 mgm. daily. Hospitalized patients have received up to 300 mgm. a day; but more than 100 mgm. daily is not recommended.

Miscellaneous Agents Not Classified as Antidepressants

Minor or major tranquilizers are often helpful in depressive syndromes; used alone or conjointly with antidepressants, they benefit anxious or agitated patients who are also depressed. Achieving a satisfactory dosage is relatively easy and safe with the minor tranquilizers. Members of this group include meprobamate (Miltown, Equanil), chlordiazepoxide (Librium), diazepam (Valium), and hydroxyzine (Vistaril). Other minor tranquilizers are equally suitable. Common side effects are drowsiness, ataxia, skin eruptions, blurred vision, and with some agents, blood dyscrasias. Habituation and withdrawal symptoms (seizures) have been reported with a number of these agents.

Benactyzine (Suavitil) is difficult to classify; chemically similar to the minor tranquilizers, it appears to possess some mild antidepressant properties. When given alone, dosage is 1 to 3 mgm. daily; however, a combination of this agent and meprobamate (Deprol) appears to be of some benefit in mild depressive conditions. Alone or in combination with other agents, benactyzine appears to be only slightly beneficial[66,69] in classical depressive syndromes, but it may be fairly effective in common grief reactions.

Deanol — Another stimulant used in mild depressive conditions is deanol (Deaner). A tertiary amine differing only slightly from choline, this compound passes the blood-brain barrier and, theoretically, should be an active central nervous system agent. Unfortunately, it is only slightly antidepressive[69,70] and has been reported beneficial only in uncontrolled clinical trials. It does appear to be of some use in certain cases of mental defectiveness and in childhood behavior disorders. It is slow-acting, and the usual daily dosage is 50 mgm. Serious side effects are rare, but muscle tenseness, insomnia, pruritus, postural hypotension, constipation, and weight loss have been reported,

Antischizophrenic — The major tranquilizers are potent antipsychotic agents, and some are effective either alone or as adjuvants in the treatment of certain depressive syndromes. With a few exceptions, these agents have equal antipsychotic action;[71,86-90] differences are in degree of sedation offered, type and incidence of side effects, and possession of antidepressant properties. It appears that two members of the phenothiazine group are less effective than the others — promazine (Sparine) and mepazine (Pacatal). The three major groups of the phenothiazines are: (1) dimethylaminopropyl, (2) piperazine, and (3) methyl-piperidyl.[4]

The dimethylaminopropyl group offers the greatest sedation; this group is comprised of chlorpromazine (Thorazine) and triflupromazine (Vesprin). These drugs should be used cautiously in depressive disorders, as reports indicate they may occasionally intensify depressive symptoms.[72] However, one of them might prove useful in certain atypical schizophrenic psychoses (schizo-affective-type) or in profound psychomotor agitation.

The piperazine group is comprised of prochlorperazine (Compazine), trifluoperazine (Stelazine), perphenazine (Trilafon), fluphenazine (Prolixin, Permitil), thiopropazate (Dartal), acetophenazine (Tindal),

Continued

and carphenazine (Proketazine). These compounds have higher activity per milligram and fewer sedative properties than the dimethylaminopropyl compounds. Extrapyramidal symptoms are very common, but these agents are very useful adjuvants to the antidepressants. Also, some of them (trifluoperazine,[73] fluphenazine,[74] acetophenazine[75]) have been reported to have mild antidepressant properties. In any case, drugs of this class can be used alone or conjointly with antidepressants in agitated depressive syndromes.

The only member of the methyl-piperidyl group in wide use at present is thioridazine (Mellaril). This agent possesses a higher milligram potency than chlorpromazine and has no appreciable incidence of extrapyramidal symptoms. Thioridazine (Mellaril) has been studied most intensively and is useful alone or in combination in the depressive syndromes.[76,84,91]

Chlorprothixene (Taractan), another agent which resembles the phenothiazines, occupies an intermediate position between the major and minor tranquilizers and has been reported to have antidepressant properties.[77] Indications for its use as an antidepressant are disputed,[78] but it may benefit certain anxious and tense individuals. Side effects are similar to those of the phenothiazines.

The Rauwolfia Drugs (reserpine) are absolutely contraindicated in the depressive syndromes or in any medical illness complicated by depression.[79] These agents have some antipsychotic activity, but they also accentuate and perhaps cause certain severe depressive illnesses. In any case, these drugs are not as generally effective as the phenothiazines.[80]

Side Effects

Common side effects of the phenothiazines include blurred vision, dry mouth, constipation, weight gain, edema, vivid dreams, and, in high doses, seizures. Extrapyramidal symptoms, including pseudoparkinsonism, motor restlessness, opisthotonos,* and oculogyric* crisis are not uncommon, especially with agents in the piperazine subgroup. Jaundice, impotence, urinary retention, dermatologic disorders, and blood dyscrasias have been reported with various phenothiazines.[81] The usual problems in prescribing these agents are insufficient dosage and failure to recognize early extrapyramidal symptoms. Only clinical experience with several provides the acumen necessary for proper determination of adequate, safe dosage schedules.

Method of Application

The first consideration in using antidepressant drugs is to arrive at a satisfactory treatment diagnosis. Though psychiatric diagnoses are vague and consensus hard to achieve, rough categories of depressive syndromes do offer guidelines to drug choice. Of course, what follows is only one of many approaches, and there are always exceptions to the outline of syndromes and the suggested treatments. More importantly, the drugs are most effective when used with psychotherapy and are not substitutes for the hospitalization and electroshock that the desperately ill patient requires.

Grief Reaction and Depressive Syndrome

As a symptom, depression is a part of grief reactions and classic depressive syndromes and is accessory to other functional and organic syndromes. *Grief reactions* are common experiences that occur following loss, and the kinds of losses possible equal the variety of things we care for — health, loved ones, possessions, etc. Grief reactions may occur at all ages in all individuals and are associated with sadness, crying, remorse, and anger. In most people the loss and feelings associated with it are intimately connected, and individuals experiencing loss often avoid anything that reminds them of it. They describe waves of sadness and remorse on thinking about the trauma, but after a variable period, the process of mourning eventually ends. Strictly, a grief reaction is not a depressive syndrome, but it may precede a depressive illness.

True or classical repressive syndromes are differentiated from grief reactions and from each other by symptoms, premorbid personality characteristics, acuteness of onset, age, and clinical course. Psychiatrists describe these illnesses in a number of ways, but for purposes of drug therapy, a classification is here adapted from a number of sources.[82,83] It is stressed that the four syndromes are approximations for treatment purposes and not substitutes for official psychiatric nomenclature.

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*See Test Your Word Score Page 1167.

Endogenous Syndrome

The first depressive pattern is termed the *endogenous syndrome* because symptoms occur in the absence of environmental disasters or, more commonly, are disproportionate to the precipitating crisis. Individuals with this syndrome have a dismal, hopeless outlook and severely impaired self-esteem. They relate profound guilt feelings and are usually withdrawn, isolated, and apathetic. Slow in speech and thinking, they complain bitterly about difficulty in concentrating. Though most psychological processes are retarded, their motor behavior may be agitated in spite of slowness in thinking, difficulty in concentrating and trouble in making decisions. They often have multiple physical concerns but are not in the truest sense hypochondriacal. Generally, the family describes the patient as "having given up" after a loss or internal conflict. The premorbid personality is often compulsive or cyclothymic.* If it is compulsive, the likelihood of agitation is greater; if cyclothymic, motor retardation is more likely. The symptoms have an insidious onset over a year or less, and frequently biological symptoms of depression (anorexia, weight loss, insomnia of the repeated-wakening type, and fatigue which is worse on arising) occur very early. This syndrome is rare before age 25; but from ages 25 to 40 it is commonly diagnosed as depressive reaction if it is not severe, and as either psychotic-depressive reaction or manic-depressive reaction (the latter if the premorbid personality was cyclothymic). After age 40, compulsive individuals are especially prone to experience their first serious depression and are frequently diagnosed as having an involutional psychotic reaction. Spontaneous remissions occur, but usually only after months or years.

Repressed Rage Syndrome

The second depressive pattern, frequently follows a sustained or major life upheaval. Repressed rage is mobilized and is frequently directed towards a loved one; sometimes this rage is not expressed, or, more commonly, it miscarries and appears as general irritability and annoyance over trifles. Such patients are also dismal and hopeless, with little self-esteem, but they are also anxious and may have other neurotic symptoms, such as phobias. Not uncommonly agitated, they make frequent clinging demands for attention. Biological symptoms of depression occur only after the syndrome is severe. Crying is frequent (in contrast to the *endogenous pattern*), and the physician has less trouble making a diagnosis. Premorbid personality usually is grossly normal, and the history suggests rather adequate adjustment before the upheaval which released the repressed aggression. Duration of symptoms prior to seeking help is usually a month or less. This pattern can occur throughout life but is frequent between the ages of 20 and 35. Commonly the pattern is diagnosed as depressive reaction or, if severe or if suicide is a feature, psychotic-depressive reaction. Occasionally, environmental situations will be such that symptoms persist for years (as in chronic-depressive reaction). Symptoms often remit spontaneously after three to six months.

Pseudoneurotic Schizophrenic Syndrome

Individuals suffering from the *latent or pseudoneurotic schizophrenic syndrome* have a long history of persistent multiple neurotic complaints (phobias, obsessions, conversions, dissociative states) and many bizarre, uncommon physical concerns. They are prone to bouts of anxiety, and their illnesses usually have variable amounts of depressive overtones. Attention to others and the world in general is reduced, and a mono-ideational concern with themselves and their bodily functions is often present. Duration of symptoms is hard to determine, since the usual

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*See Test Your Word Score Page 1167.

history is a lifelong pattern of distress. Age of onset varies, but frequently the diagnosis can be made in the twenties, although for decades these individuals may appear neurotic or to have a bona-fide physical ilness.

Maladjusted Personality

Individuals who show the *maladjusted-personality-with-depression pattern* have a long history of personal maladjustment and are often at their best demanding, provocative, angry, and resentful. They are basically narcissistic and overaggressive individuals who dominate others by active or passive means. When thwarted, denied, or frustrated, or unable to continue their usual behavior, they become depressed, and not uncommonly their depression is used to influence the environment. Suicidal threats, thoughts, and attempts are common, and the patient is hard to treat, since impulsivity and destructiveness may be directed toward others. These individuals represent various personality disturbances including passive-aggressive, inadequate, psychopathic, and emotionally unstable personalities. Symptoms are acute in onset (usually a month or less) and often occur precipitously over several hours or days. Biological symptoms are rare unless the illness progresses for some time. The duration of symptoms depends on the environmental circumstances, but usually they last six weeks or less. They occur at all ages in such individuals, but are most frequent between the ages of 15 and 25.

The Choice of Drugs

Using the above classification, some rough rules may be applied to drug choice. *Grief reaction* is not a true depressive syndrome and seldom requires a potent antidepressant. One of the direct stimulants (amphetamines), deanol, or benactyzine can sometimes be helpful as an ancillary to compassion and support. Drug choice in the endogenous syndromes depends on psychomotor symptoms.

Quite *agitated and anxious patients* usually respond best to a central nervous system suppressant, and retarded, apathetic and generally slowed-down patients do best on an indirect or bimodal central nervous system stimulant. If other therapies fail, agitated patients can be tried on an indirect or bimodal stimulant in combination with a phenothiazine.

Depressions of *the suppressed-rage type* often fail to respond to antidepressants alone or are more benefited by a barbiturate or ataractic.* A good policy is usually to start therapy with a minor tranquilizer or a mild phenothiazine (chlorprothixene) for several days to one week. If the patient does not respond, one may then try either a central nervous system suppressant or an indirect stimulant in association with the tranquilizers.

Patients with latent or *pseudoneurotic schizophrenic syndromes* are best treated by a trial of a phenothiazine (trifluoperazine, fluphenazine, perphenazine, thioridazine, etc.) followed in several weeks by an adequate dosage of a bimodal or an indirect stimulant. This treatment should be continued for months to years.

Patients with a *maladjusted personality syndrome* should be handled with extreme caution; usually minor ataractics should be tried and the patient seen often (twice a week) before initiating an antidepressant. Because of their unreliabiilty, these patients probably should not receive monoamine-oxidase inhibitors of any kind but should be maintained on the central nervous system suppressants.

Depressions associated with other illnesses, both functional and organic, are best treated with central nervous system suppressants alone or in combination with ataractics. Occasionally an indirect or a bimodal stimulant may be helpful if there are no medical contraindications.

In combination therapy a good rule is to start one drug at a time. If a patient is anxious, fearful, or phobic, an adequate dosage of a minor tranquilizer is helpful. If he has agitation without psychological content (fear, phobias, etc.), a phenothiazine often helps. In a schizophrenic disorder, one should never give an antidepressant outside a hospital without the protection of a phenothiazine. It is best not to give more than one tranquilizer and one antidepressant, as multiple agents interact adversely, and if an untoward effect occurs, one cannot determine which drug is the offender.

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*See Test Your Word Score Page 1167.

General Considerations of Treatment

Beyond the choice of drugs, one must consider the general pattern and means of treatment. Generally, one should see patients at least twice weekly at the beginning of therapy, both to supervise medications and to prevent suicide. Depressed patients are quite prone to disastrous despondency if therapy fails. In a patient in whom the role of depressive elements is in doubt, it is best to treat tense, restless and anxious symptoms with a minor ataractic and wait three or four days until the patient has a chance to collect himself. On occasion this is sufficient and the illness will abate spontaneously. If you are doubtful about the patient's reliability, avoid the monoamine-oxidase inhibiting drugs and use a central nervous system suppressant. In adequate dosages the central nervous system suppressants have a wide spectrum of activity and are the safest agents for older patients. After receiving adequate dosages for several weeks, there should be some relief of symptoms. If not, the patient should be reevaluated and hospitalization considered. If he is doing well, then weekly visits for three to four weeks (continuing the previous dosages) should be tried. By then the patient should be in reasonably good health, and maintenance therapy can be initiated. Maintenance therapy should continue for about three to six months, and the dosage gradually decreased during this time. After six months, one must try to discontinue at least the antidepressant (except in latent schizophrenic individuals). Occasionally chronic depressive reactions require longer therapy, but these are rare in general medical practice.

Abuses

The chief abuse in the use of antidepressant drugs is to prescribe large quantities for people who don't need them. A physician should not hesitate to discontinue all therapy in depressed patients after three to six months, unless he is reasonably sure the patient is chronically depressed. Another flagrant abuse is concomitant treatment with too many ancillary therapies. Not rarely patients receive one or more antidepressants, several tranquilizers, two or three analgesics, and several hypnotics at the same time. Since most patients with depressed syndromes have real potential for suicide and since the interaction of all these agents is fraught with many physiological difficulties, one should limit the therapy of a depressed patient to one antidepressant, one tranquilizing agent, and one hypnotic.

These agents are also abused in their use for the elderly. Senescence is a severe problem often accompanied by many untoward life experiences, and antidepressants are frequently ineffectual and actually dangerous because of their side effects. Chloral hydrate or a minor tranquilizer in conjunction with judicious counseling and placement will often accomplish more in the elderly than antidepressant medications. In regard to referral, it is best to refer any patient who has threatened suicide. Moreover, one should refer any patient who does not get better within three to six weeks. Depressive syndromes generally begin relenting fairly early in the course of therapy, the only exception to this being that some central nervous system suppressants and indirect stimulants take several weeks to work.

Summary

Antidepressant drugs are indicated for central nervous system stimulants or central nervous system suppressants, but general precautions should be observed in prescribing these drugs in specific disorders.

Acknowledgment

The author is indebted to Dr. B. C. Schiele for his advice and criticism.

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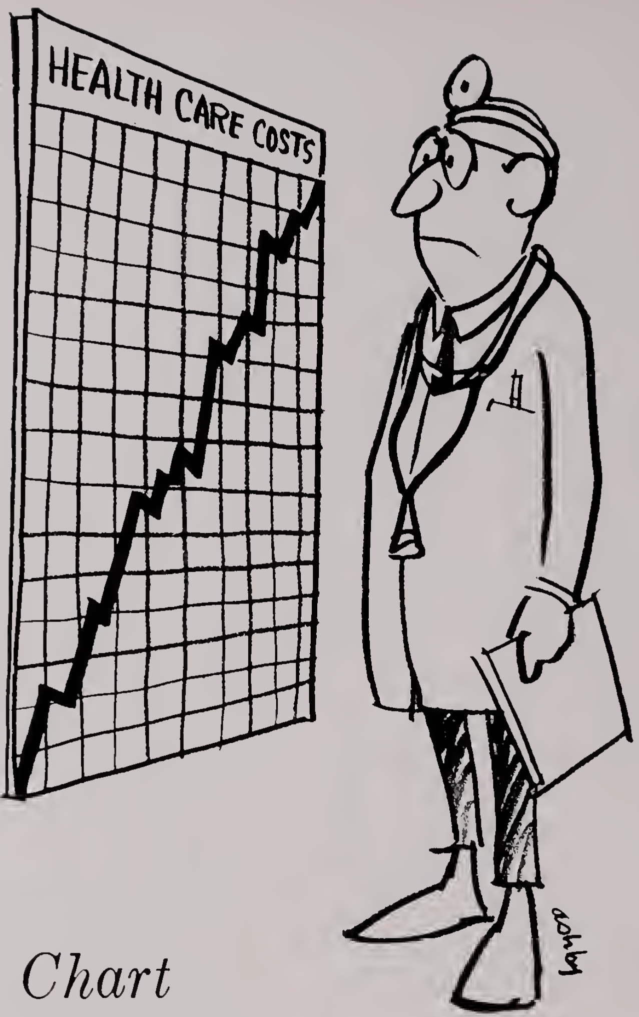
3-96. May be obtained from the author or the reprints.



Fever Chart

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Abstracts, Briefs and Commentaries

MANAGEMENT OF MALIGNANT PLEURAL EFFUSION

Kinsey et al. obtained good results in the treatment of malignant pleural effusion by the instillation of 30 mg. of mustrogen hydrochloride diluted in 150 cc. of isotonic saline. They instilled this into the pleural cavity with a tube, left it for several hours and then removed it. Eighty-seven per cent of their cases were adequately controlled, and in the group of 62 patients the survival time was extended 11.6 months in those patients whose malignant pleural effusion was due to carcinoma of the breast.

The procedure is simple, requiring no special equipment, merely a small trochar and the insertion of a catheter in the pleural space where it is left until the treatment is finished. The effusion is first removed, the mustrogen is then instilled, and that too is removed after several hours. This may offer a possibility for a patient requiring repeated pleuracentesis in order to obtain comfort in breathing.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Kinsey, Dave L., Carter, Daryl, and Klassen, Karl: Simplified Management of Malignant Pleural Effusion. Arch Surg 89:389, 1964.

PRIMARY LYMPHOMA OF THE THYROID GLAND

The literature on primary lymphoma of the thyroid gland is reviewed, and nine additional cases are presented. In view of the longevity statistics (patients with primary lymphoma of the thyroid gland living from four years up to 18 years in one case), one should consider the prognosis to be more favorable than heretofore quoted. The current therapy for primary lymphoma of the thyroid gland depends upon whether the disease is localized, invasive, or disseminated. Several authors have stated that a probable relationship exists between lymphoma and lymphomatous thyroiditis (Hashimoto's disease), but statistically it cannot be held significant considering the number of cases of Hashimoto's lymphomatous thyroiditis treated throughout the world.

Courtesy of References and Reviews
Journal of the American Medical Association

Mikal, S.: Surgery 55:233, 1964

APPENDICITIS IN PREGNANCY

In 74,000 obstetrical patients admitted to Los Angeles County Hospital between 1957 and 1961 the incidence of acute appendicitis in pregnancy was 0.05 percent. A study of 36 cases clinically diagnosed as appendicitis in pregnancy showed that the fetal and maternal morbidity and mortality were reduced when a definite operation was done early.

The difficulty of diagnosis is increased in these cases by the need to consider pyelonephritis and twisted ovarian cyst.

Rupture of the appendix reduced the chances of maternal and fetal survival. Threatened premature labor may indicate a ruptured appendix. In such cases an emergency operation with the use of antibiotics was effective.

The incidence of premature delivery was proportionate to the delay in operating. If operation was performed within eight hours of admission there was no maternal or fetal loss. A delay greater than eight hours resulted in a 17 percent fetal loss in premature deliveries and a 4 percent loss of infants at term.

Courtesy of World-Wide Abstracts

King, R., and Anderson, G.: Calif Med 97:3,158

REVERSAL OF RENAL HYPERTENSION

Griffiths and Schwartz have indicated that there are four major baroreceptor areas, two in the carotid sinuses and two situated in the aortic arch. The central nervous system serves as the afferent limb of the baroreceptor reflex and transmits to the vasomotor center the action potentials from the carotid sinuses, as these areas have been considered to be stretch receptors and are presumably activated by the intraluminal pressure of the carotid artery, which, when stimulated reflexly, lowers the blood pressure, induces bradycardia, increases cardiac output, and diminishes venous return. The converse situation is noted when the pressure within the receptors is lowered.

These authors, using an electrical stimulus to the carotid sinus area of the dog, were able to observe a reduction in the hypertension which had been experimentally induced.

The clinical application of this electrical stimulation of the central nervous system, as a method of reducing blood pressure in hypertensive patients, is being done, and merits further study.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Griffith, Lawrence S. C., and Schwartz, Seymour I.: Reversal of Renal Hypertension by Electrical Stimulation of Carotid Sinus Nerves. Surgery 56:232, 1964.

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POSTMYOCARDIAL INFARCTION SYNDROME

The features of the postmyocardial infarction syndrome are presented, and the radiographic findings in 11 cases are reported, with 2 cases being described in detail. It is important that the syndrome be promptly recognized, not only so that proper therapy can be instituted, but to prevent improper therapy that may prove fatal. Radiologists should be aware of this newly recognized complication of a myocardial infarction since the condition may be first suspected from radiographic findings, and because it offers another explanation for the nonspecific findings of cardiac enlargement, pneumonitis, and pleural effusion. The syndrome is easily confused with an extension of the original myocardial infarction, heart failure, and pulmonary infarction. The etiology is not known. Treatment is discussed.

Courtesy of References and Reviews
Journal of the American Medical Association

Shopfner, C.: Radiology 81:236, 1963

L. E. CELLS IN LYMPHOMA

Positive lupus erythematosus (LE) cell tests were obtained in two elderly women with lymphoma: the necropsy diagnoses were lymphosarcoma and Hodgkin's disease respectively. In the patient with lymphosarcoma, the LE cell test was positive on 24 occasions, and positive results were obtained in tests for thyroglobulin antibody and rheumatoid factor: treatment with radioactive phosphorus was beneficial. The Coombs test was positive in both patients. The origin of antinuclear and other autoantibodies in these cases was attributed to the development of self-reactive "forbidden" clones of lymphoid cells as a consequence of neoplastic change in lymphoid tissue. Lymphomatous conditions with autoimmune features could represent release of a range of abnormal clones of lymphoid cells, in line with Burch's concept that leukemia is dependent on a combination of germinal and somatic mutation.

Courtesy of References and Reviews
Journal of the American Medical Association

Howqua, J., and Mackay, I.: Blood 22:191, 1963

READABLE WRITING

Busy physicians do not have time to wade through tediously written material. Too many complex words and too many long, involved sentences produce reports that might be best described as scientific gobbledegook. Writing ought to be simple and clear. The reader will read more, in less time, and understand better. Medical writing does not have to be stuffy or dull. It would be more interesting and useful if authors would use plainer words, shorter sentences, more compact paragraphs, and more direct style.

Courtesy of References and Reviews
Journal of the American Medical Association

LeCron, L.: Northw Med 52:264, 1963

SMALL-BOWEL NEOPLASMS: ELUSIVE SOURCE OF ABDOMINAL SYMPTOMS

The surgical records and autopsy findings of 78 patients with primary small-bowel neoplasm are analyzed in an attempt to define the diagnostic problems presented by such neoplasms and to suggest methods of treatment. Malignant lesions were present in 74.4% of 43 symptomatic cases. The symptoms included nausea and vomiting, abdominal pain, abdominal tenderness, intestinal obstruction, palpable mass, intestinal hemorrhage. The diagnosis was established preoperatively in 53% of symptomatic cases by X-ray examination. Most of the failures in diagnosis occurred because a possibility of small bowel tumor was never considered in the differential diagnosis. In a few cases, laparotomy is the only diagnostic recourse; it is justified when the patient's case has been properly evaluated and roentgenograms have been revealing, but suspicion exists.

Courtesy of References and Reviews
Journal of the American Medical Association

Strauch, G. O.: Surgery 55:240, 1964

PITFALLS IN THE DIAGNOSIS OF PANCOAST TUMOR

The Pancoast syndrome is a well defined one that may have a longer clinical history than was previously believed. Four of the author's 11 patients had a history of over six months, and two had a history of at least two years. With recent improvement in therapy, significant cure and palliation can be accomplished, and an earlier diagnosis may better the results. With routine chest films, seven of the 11 cases were not diagnosed. With the addition of an anteroposterior spine film and apical lordotic and oblique films of the apices, however, all were readily recognized. Six patients had bone destruction, and five a soft-tissue mass only. It was surprising how much bone destruction could be missed on a routine chest film. Fluoroscopy with barium contrast along with laminagrams, added to the diagnostic study. If there is a suspicion of a superior sulcus tumor, routine chest films, and anteroposterior dorsal spine roentgenograms, and lordotic views should be the minimal examinations, and with these very few lesions will be missed. If these measures are not diagnostic, additional special studies should be performed.

Courtesy of References and Reviews
Journal of the American Medical Association

Simon, H., Moon, A. C.: Radiology 82:235, 1964

HOW TO TELL GIRL ABOUT MENSTRUATION

Since doctors often are called upon to give guidance and information to families and young girls, copies of "How to Tell the Retarded Girl About Menstruation" may be obtained by doctors, parents, guardians and educators by writing to the Educational Department, Kimberly-Clark Corporation, Box 551-MRB, Neenah, Wisconsin.

The word "retarded" should have been deleted from the title, as the information within the pamphlet is of value to all girls.

Carl O. Rice, M.D.
Minneapolis, Minnesota

CRITIQUE OF THE VIEWS OF DR. THOMAS SZASZ ON LEGAL PSYCHIATRY

Dr. Szasz, a professor of psychiatry at the State University of New York (Syracuse Branch) has become a reckless public critic of organized psychiatry and indirectly of organized medicine. He maintains that there is no such thing as mental disease and is a proponent of individual freedom that goes beyond the limits of reason and practicality. In fact, he would do away with all enforced psychiatric hospitalization and would allow individuals full liberty to injure themselves, even to the point of suicide. While it is true that abuses can and do occasionally occur in commitment procedures and during psychiatric hospitalization, they will not be prevented by the intemperate writing of Dr. Szasz, which is marked by gross distortions and inaccuracies. Although some of the views expressed in his latest book are provocative, it performs a great disservice by needlessly alarming the families of hospitalized patients and by providing the ill-informed critics of psychiatry with inaccurate data and specious theories.

Courtesy of References and Reviews
Journal of the American Medical Association

Guttmacher, M. S.: Arch Gen Psychiat 10:238, 1964

HODGKIN'S IN PREGNANCY

A review of 35 cases of pregnancy associated with Hodgkin's disease revealed that in 28 women the disease was discovered during pregnancy, in 18 during the first trimester. Of the total number, 28 were delivered normally at term. Four of the pregnancies were terminated early by spontaneous abortion, all in patients who had become pregnant after the onset of the disease. No stillbirths or congenital anomalies occurred. A surprisingly large number of patients failed to become pregnant a second time. Pregnancy did not affect survival time; however, it was shorter in patients over 35 years of age as compared with the survival time of those under 35, regardless of whether they previously had children or not. No evidence was found that gestation accelerated the course of the disease. Interruption of pregnancy is not indicated on the basis of evidence presented in this series.

Courtesy of References and Reviews
Journal of the American Medical Association

Hennessy, J. P., Rottino, A.: Amer J Obstet Gynec 87:851, 1963

For 'Stinking Ulcer'

The ancient Egyptian pharmacopeia contained numerous remedies for 'stinking ulcer.' The following salve is intriguing less for its bizarre ingredients than for its appended tag of solicitous advice.

"ANOTHER REMEDY TO DRIVE OUT A STINKING ULCER IN THE BODY OF A MAN OR WOMAN:
Egg-of-an-Ostrich
Tortoise-shell
Thorns-of-the-am-tree
Warm and anoint therewith.
BUT DON'T GET TIRED DOING IT!"*

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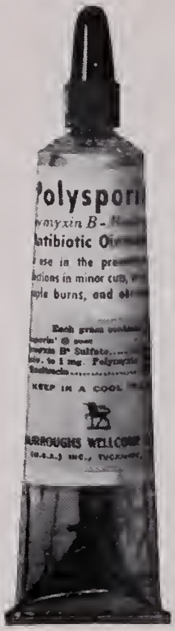
*Bryan, Cyril: The Papyrus Ebers, D. Appleton and Company, New York, 1931, p. 74-75.

in treating topical infections, no need to sensitize the patient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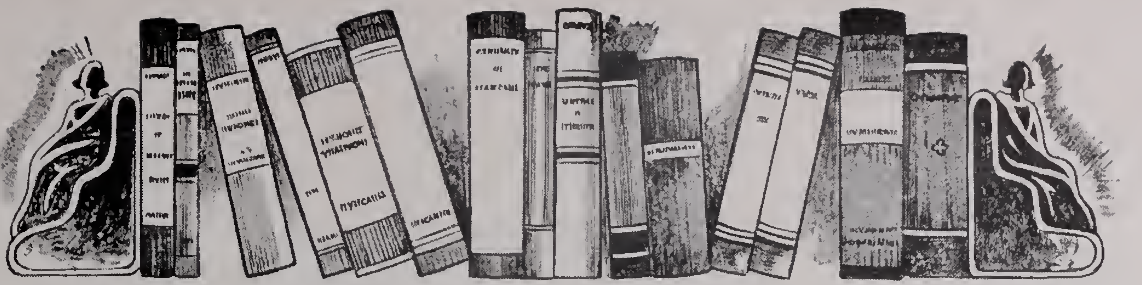


Book Reviews

Laws die, books never. — Bulwer-Lytton

STEREOSCOPIC MANUAL OF THE OCULAR FUNDUS IN LOCAL AND SYSTEMIC DISEASE — F. C. Blodi, M.D. and L. Allen, M.D., St. Louis, C. V. Mosby Co., 1964. Illustrated, including 105 stereoscopic color photos and viewer, index. Price $32.50.

The authors have developed a simple method of taking stereophotographs of the ocular fundus by slightly rotating the Zeiss fundus camera for the second exposure. This volume supplies the fruits of their labor for armchair viewing with the collapsible instrument included. There are 15 viewing reels, divided into various disease categories such as hypertension, tumors, diabetes, etc., covering the high points of most eyeground changes seen, not only by the ophthalmologist but by the internist, neurosurgeon, or anyone who has occasion to use the ophthalmoscope. Accompanying each view is a description of the patient and the disease, many of the descriptions accompanied by black and white photomicrographs of the histopathology, enabling one to get a good idea of the correlation of gross and microscopic pathology.

This is a truly beautiful medical book and is a delight to own and browse through.

W. S. McClanahan, M.D.
Minneapolis, Minnesota

MARRIAGE COUNSELING IN MEDICAL PRACTICE — edited by Ethel M. Nash, M.A.; Lucie Vessner, M.D. and D. Wilfred Abse, M.D. and published by the Van Rees Press, New York, 1964.

The title of this book, "Marriage Counseling in Medical Practice," tells exactly what this book is about. It is a symposium written by a group of authors who in general do an excellent job from the viewpoint of the practicing physician with a difficult subject.

This book is of value to any physician regardless of specialty or interest, and particularly to medical educators in order to aid them in focusing their attention on the preparation of medical students and doctors in the area of marriage conflict. Marital problems are frequently the basis for many symptoms which bring patients to physicians. The book will help the physician handle more effectively some of the problems that result from marriage conflict, but more important, it may make him anxious enough to agitate for more facilities to better train him in the field of marriage counselling.

Even for the psychiatrist, who is probably the best trained of all physicians in the area of marriage counselling, this book has much to offer, although some may disagree with some of the ideas presented in the book.

Irving C. Bernstein, M.D.
Minneapolis, Minnesota

"SIGNS AND SYMPTOMS" — Cyril Mitchell MacBryde, J. B. Lippincott Co., 1964. 971 pages.

This is the Fourth Edition of MacBryde's "Signs and Symptoms."

The word symptom is used to name a manifestation of disease, which is usually a subjective observation from the patient.

Pain being a significant sign, the book contains eight chapters dealing with pain, originating from the various sections of the body. By using the table of contents, the reader is able to guide himself into the proper chapter, which may be of interest to him at the moment.

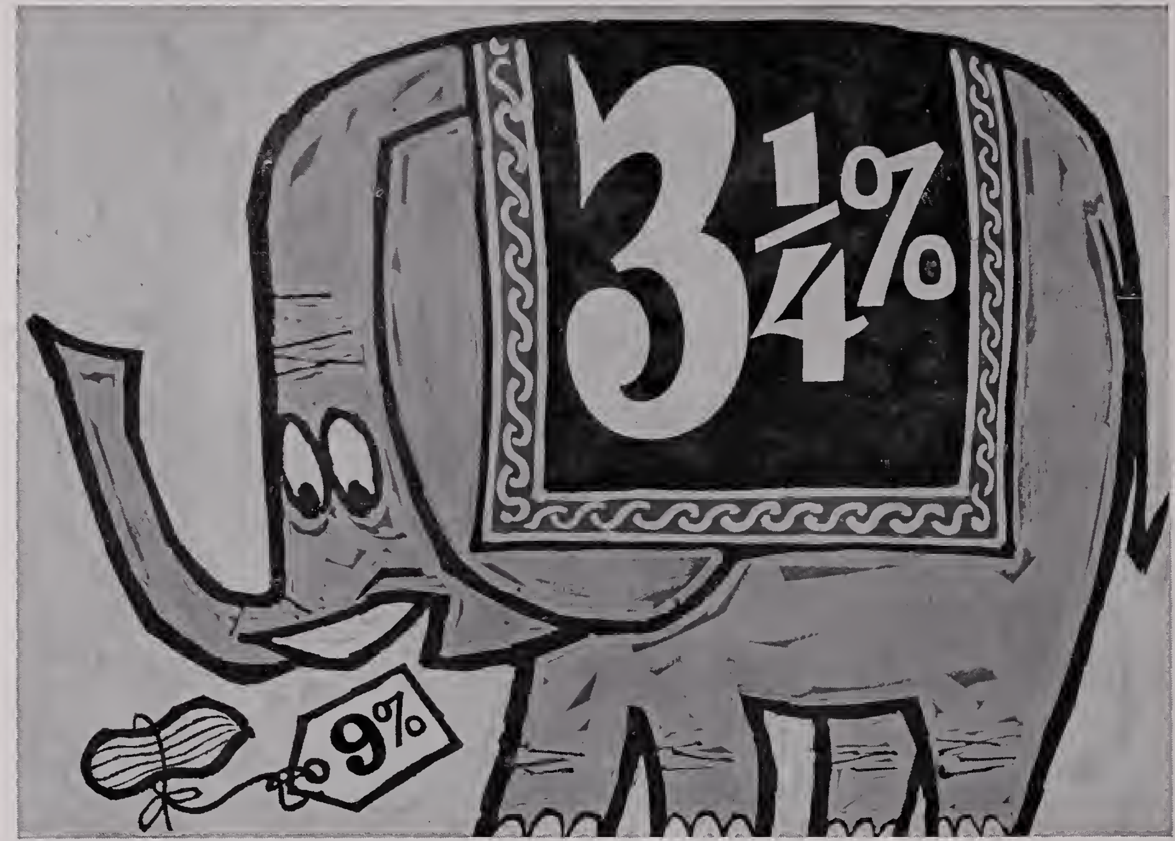
Generalized vasospasm, tachycardia, cough, hemoptysis, dyspnea and cyanosis direct the reader to a series of chapters devoted principally to cardiovascular and respiratory disease, and then there are a series of signs which direct one to the diseases of the gastrointestinal and biliary system.

Bibliographical references are tendered at the end of each chapter and these, though not extensive, seem to be adequate for more specific reference to the contents within each chapter.

I have found this to be an excellent edition, as a reference for a large variety of signs and symptoms that one encounters from day to day.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Riddle:
When is 3¼% larger than 9%?



Answer! When it represents *keepable* income from tax-free municipal bonds! A 9% yield from ordinary stocks may seem like a nice profit. But, it's really small peanuts, if you're in a high income bracket. Reason? Federal and state income taxes can take a huge amount of that profit away. Not so with *tax-free* municipal bonds! They allow you more "keepable" income . . . more big peanuts to salt away in your trunk! First National Bank offers a large selection of these bonds. Sound good? Then mail the coupon below for our free booklet "The Story Behind Municipal Bonds," as well as our handy "Tax Exempt Versus Taxable Income Table." Both give you vital information that can save you money. Or call our Investment Department (221-9463). So make like an elephant—don't forget—tax-free bonds can give you more *keepable* income!

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Special Article

Vignettes of the Surgical Horizon and the Surgeon's Image

New and Old*

OWEN H. WANGENSTEEN, M.D.**
Minneapolis, Minnesota

Anyone and everyone who offers a paper for presentation is offering himself as well as his ideas for inspection by his Fellows. I am always intrigued and stimulated by the young man who makes an all-out effort and comes up with a mature presentation of his assigned subject. When he passes the inspection with credit, he receives at the hands of his associates enhanced opportunities for growth and development.

Such inspection is a recurrent and lifelong process. At my time of life, after many years amongst you, perhaps the only useful purpose served by my appearance tonight is to provide you with an opportunity of advising whether I am ready for superannuation. Oliver Wendell Holmes once said, "Old age calls on us at age 50 and leaves his calling card." I have accumulated almost a "full house" of such cards, but the satisfactions of study and application are so pleasant and rewarding, I have resisted any summons to retire from the professional scene, even though the beckoning voice of the vesper bell of retirement occasionally titillates my eardrums agreeably.

However, my being with you tonight offers me the unique opportunity of indicating to the surgical profession of this community my deep appreciation of years of devoted and selfless service by many of its members to the Medical School and its Department of Surgery. And to all of you, I want to say on behalf of the School and particularly the Department, how very grateful we are that over long years the school has had and continues to have the confidence and the support of the profession. It has been pleasant to work in an environment in which the stimulus and the support of friends continually urge one to do his best. It was, therefore, with a sense of high privilege that I accepted your gracious invitation to be with you tonight.

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*Presented at the Annual Meeting of the Minneapolis Surgical Society, April 7, 1965.

**University of Minnesota Medical School, Department of Surgery, Minneapolis, Minnesota 55455.

Continued

My entire professional life has been spent within the walls of a university. This discussion, therefore, will reflect the bias and the limitations of one who has not been exposed to the give-and-take of medical practice as most of you have. Even so, our problems in many particulars are probably very much alike.

My primary role has been that of conducting the affairs of a rather large clinical department, to teach undergraduate medical students, to supervise the instruction of graduate students in surgery and to integrate the professional services of a complex staff working in several satellite institutions. It has been a unique and wonderful opportunity, which, after all, is a professor's best paymaster.

My role has essentially been that of sideline cheerleader and regimental water carrier, but my most important function, I have come to believe, has been in trying to create an atmosphere sympathetic and friendly to learning—an environment in which scholarship and industry thrive, bringing out the best latent qualities of men. Men and the proliferation of ideas, emerging and generated in such a milieu, almost invariably prove to be every teacher's greatest discovery.

Changes on the Professional Scene

Senior, as well as latter-day general surgeons, are well aware that the surgical arena is changing. The surgeon of my training days was schooled to believe he could learn to do most operations reasonably well. With the advent of the many specialties of neurosurgery, orthopedics, urology, proctology, plastic, thoracic, and intracardiac surgery, he has come to realize that colleagues in all these related responsibilities achieve a level of competence to which the general surgeon cannot pretend. All surgical specialties now appreciate the importance of research in the training of surgeons. Over a number of years, I have been convinced that our best surgeons are products of the experimental laboratory. The time will certainly come when the young surgeon will acquire his primary surgical skill in the laboratory rather than on the wards, as is still current practice. When a young surgeon has demonstrated his skill in operating on the dog, he is ready for operations on man. A distinguished British surgeon remarked some time ago, while visiting our laboratories, what a great advantage the young American had in the opportunity to become a reasonably accomplished surgeon before making his first incision into human flesh.

Today surgeons do not suffer any embarrassment over taking a long time to do an operation well. Up until the beginnings of World War II, the time factor was a matter of the greatest concern in the performance of all operations. I was privileged a few years ago to watch a well-known Norwegian surgeon operate for coarctation of the aorta. After applying the hemostatic clamps, he took a twenty-minute period for refreshment before addressing himself with superb skill and energy to making a nice arterial anastomosis. Forty years ago, such behavior certainly would have resounded throughout the hospital and become a matter of common public knowledge in the surgical community before the day was out.

Many changes have occurred on surgical wards over the past five decades since World War I. As recently as three decades ago, patients with empyema, osteomyelitis, and goitre were frequent occupants of surgical wards. The effectiveness of antibiotics virtually eliminated the first two. Implementation of Marine's thesis that goitre is essentially an iodine-deficiency disease has made cancer, rather than exophthalmic goitre, the most common surgical thyroid disease. Tuberculosis of bones and joints and tuberculous lymph nodes have disappeared from the scene, largely as a consequence of pasteurization of milk and the slaughter of diseased cattle. Pulmonary tuberculosis too, which usurped the attention of the thoracic surgeon three decades ago, has almost vanished from hospital wards as a consequence of isolation, streptomycin, and pharmacologic adjuvants.

Patients with acute appendicitis today, well cared for in their own communities, are now a rarity upon the wards of a University Hospital. The 95-percent decrease in the mortality of appendicitis[1] that has occurred at the national level over the past 35 years is due to earlier surgery and improvements in surgical care and appreciation of the potential hazard of luminal obstruction of the appendix which is capable of a secretory pressure approximating systolic blood pressure. The mortality of peptic ulcer perforation has been greatly lessened by timely surgery and antibiotic therapy. The persistent mortality of peptic ulcer today is essentially that of massive hemorrhage, upon which use of gastric cooling has begun to make an impress. Definitive control of the peptic ulcer diathesis awaits elucidation of a number of factors in its potentiation and the development of more effective nonoperative methods to combat acid peptic activity. Gastric freezing is often attended by dramatic early but somewhat disappointing late results. Its efficacy as an anti-ulcer agent is still on trial.

A 50-per cent reduction in mortality from bowel obstruction has occurred over the past 30 years. McKittrick and Sarris[2] (1940) reminded the profession 25 years ago that no significant improvement in the mortality of intestinal obstruction had been observed at the Massachusetts hospitals in the 50-year period beyond 1890, until introduction of better techniques of nonoperative and operative decompression and earlier surgery became the order of the day. Today in some hospitals, including our own, the hospital mortality for acute simple obstruction with viable bowel is approximately 1 per cent for the small intestine[3] and 5 per cent for the colon. Delay, strangulation, perforation and the difficult obstructions of the newborn account largely for the persistent morality. General implementation of well established techniques should presently be reflected in additional important gains detectible in our vital statistics.

Surgery of the Heart and Large Arteries

The most exciting development in surgery in the past dozen years has been in treatment of heart disease, once solely the domain of the internist. Courageous and aggressive surgeons are now repairing congenital defects of the heart in large numbers with mortalities no greater than those attending operations dealing with more prosaic lesions.

Intracardiac surgery is essentially a development of physiology and reflects the importance of training in adapting techniques from other disciplines. Simultaneous progress in angiography and telemetry came also as great and fortunate boons to the cardiac surgeon.

Heart valve replacement is an even greater challenge involving engineering skills. Imaginative surgeons are toying with mechanical pumps and small reservoir devices to replace the heart, while others have built hyperbaric oxygen chambers which may come to supplant extracorporeal circulation for a few conditions during cardiac bypass.

Pacemakers are permitting a normal life to a large number of patients. Control of blood pressure by similar means is currently under surveillance. Perhaps presently, one may see such devices available to energize respiration, to control motion in paralyzed extremities, or perhaps even to take over the complicated functions of the liver and of the kidney. If and when we learn how to prevent rheumatic heart disease and congenital cardiac deformities, cardiac surgeons will channel more thought and effort to the challenging problem of dealing with obstructions in the coronary and peripheral small arteries of the brain and lower extremities.

The cause of atrophy of the islets of Langerhans in diabetes is still a puzzling enigma. Surgical efforts directed at improving the arterial circulation of the pancreas in diabetes could prove rewarding.

Corrective surgery for replacement of large arteries has been a great achievement in the last decade, yet the basic information relating thereto had been available for nearly fifty years. Alexis Carrel was given the Nobel Prize for his important contributions to blood vessel anastomoses in 1912, an award which some modern students feel should properly have been shared by his associate, Charles Guthrie. The coming of heparin obviously played a significant role in the harvest and extension of life which has rewarded the surgeon's aggression upon degenerative diseases of major arteries.

Continued

Slow Evolution of Antiseptic Surgery

The importance of looking backward in experience as well as forward in experiment must not be forgotten. Thus, as one looks back, it is quite obvious that antiseptic surgery might well have come two decades earlier, had the mood of acceptance been warmer in 1847 when Semmelweis introduced chlorine compounds for hand disinfection. A Jacob Henle[4] (1840) and a Louis Pasteur[5] (1861) were necessary to point the way to the role of bacteria in the genesis of wound suppuration. It was the brilliant observations of Julius Cohnheim[6] (1861-73) upon leucocytic diapedesis* and filtration of fluid and cellular elements from the blood vessels at the site of injury which laid the foundations for the modern views of inflammation. Cohnheim's observations made John Hunter's[7] phlebitic theory of inflammation obsolete and similarly outmoded Virchow's[8] thesis of total participation of all tissues at the site of injury in the inflammatory process. Lister's[9] observations on compound fractures and the important work of Robert Koch[10] in separating out pure cultures of bacteria helped to make the work of Pasteur more intelligible and to break down the stubborn resistance to acceptance of antisepsis. Koch's work also hastened assimilation of asepsis into hospital practice. Reintroduction of the antiseptic spray of Lister in a new form is very much needed today, as well as new techniques of operating room ventilation to reduce the hazard of air contamination during operations.

Insulin, vitamin B_{12}, cortisone, and antibiotics are miracles of our age. It is to be hoped these significant discoveries will be matched by development of pharmacologic or immunologic inhibitors which will suppress anomalous organ function and control peptic ulcer, hyperfunction of the hypophysis, parathyroids, adrenals, and aberrant tissue growth and lend encouragement as well as accomplishment to the heroic efforts of surgeons in their attack upon the problem of homografting of organs. The stumbling block of a skein of immunologic enigmas will have to be disentangled before homografting is ready for general clinical application.

Cancer

In an address in 1897, W. W. Keen,[11] a well-known American surgeon, regretted he would not be alive in 1947, for the passage of 50 years he believed would certainly see the conquest of cancer. The late King George V proved a far better prophet. In addressing the First International Cancer Conference in 1928, the King said through his counsellors: "I note with interest that your object is research, both into the cure and causes of cancer. No doubt in the last resort the discovery of the cause is the only certain and absolute means of cure. But I am glad that you have not ignored the practical side of the problem. Remembering the thousands of sufferers from cancer, I feel that if your discussions lead to advance in diagnosis, treatment, or even palliation of the disease, this conference will have justified itself and earned the gratitude of mankind."[12] — suitable words of introduction for many a cancer conference held during intervening years.

A nearly 50-per-cent decrease in the mortality of cancer of the cervix at the national level has occurred over the last twenty-five years owing solely to a responsive public learning to appreciate the worth of the Papanicolaou Test in detecting early cervical cancer. Similarly there has been a 12-per cent reduction in the mortality of cancer of the rectum owing to acceptance in many areas of the value of an annual proctoscopic examination in the detection of early cancer of the rectum.[13] Studies of our Cancer Detection Center, an activity which has been fortunate to have had a favorable nod from the Cancer Committee of the Minnesota State Medical Society over the past 17 years, suggest that cancer of the rectum may also come to be a disappearing disease. Cancer of the large bowel, involving both rectum and colon, is the largest contributor to deaths from any organ inasmuch as it is a frequent cancer in both sexes. A similar reduction in cancer of the colon beyond reach of the proctosigmoidoscope must await development of more precise roentgenologic techniques of cancer detection. Perhaps the most surprising and rewarding finding of our Cancer Detection Center Studies is that an annual examination of the breast, in the hands of interested and experienced personnel, suffices to detect breast cancer sufficiently early so that the five-year survival amongst women in that group has been 90-per cent — a 100-per cent improvement over the current situation relating to patients arriving at the outpatient clinic of our hospital with a clinical diagnosis of breast cancer.[14] Until major breakthroughs occur that will drastically change cancer management, cancer detection clinics must be looked to as a practical and very worthwhile direct attack upon the problem of cancer.

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*See Test Your Word Score Page 1167.

I have heard Dr. Donald J. Cowling, great Minnesota citizen, when listening to narration of circumstances carrying overtones of self-service, utter the telling remark: "Noble Soul!" Any such suggestion detectible in the foregoing account will serve only to indicate that some of these gains are due to the work of my colleagues.

Inventory of Surgeons' Wishes

Among innovations, longed and hoped for, the following are undoubtedly near the top of most surgeons' wishing inventory:

1. Pharmacologic or antibacterial agents to eliminate or control pyogenic infection.
2. Simpler and more effective hemostatic agents, as well as anticoagulants.
3. Simpler and even more effective anesthetic agents.
4. Effective means of sustaining a normal circulation in shock.
5. Means of accelerating wound repair.
6. Mechanical devices to simplify operative procedures upon small tubular structures.
7. Techniques to ablate the antigenic properties of immune reactions which continue to retard development of organs.

It is undoubtedly to the interdisciplinary facets of biochemistry, biophysics, bioradiology, microbiology, experimental pathology, pharmacology, and physiology, that we must look for new tools and techniques which can make these needs a reality.

Challenging Problems

We have had the unique opportunity of witnessing a most dramatic and telling consequence of the results of research over the past decade upon a world-wide scourge. In 1953, the Metropolitan Life Insurance Company paid death benefits to the families of victims of poliomyelitis in the amount of $658,000; a decade later the outlay was $7,000.[15] How wonderful to observe the disappearance of this menacing crippler! Strange as it may seem to us in Minnesota, malaria causes more disability and takes more lives than any other disease. Tuberculosis too continues prevalent in many areas of the world, pointing up very obvious geographic differences in health problems. At the turn of the century, pneumonia and tuberculosis were reported as the first and second causes of death in the United States. Twenty years from now most infectious diseases will probably be well controlled, almost universally.

Today, heart disease in its many manifestations, cancer, trauma, and congenital deformities account for more than 75 per cent of deaths in our country, revealing what public health measures and the combined wisdom of all the health sciences have yet failed to influence significantly. At best, death can only be postponed. President Johnson's proposal of an all-out frontal attack upon heart disease, stroke, and cancer reflects the suggestion that redeployment of medical investigative talent in heavier concentration upon these diseases will cause these formidable and menacing foes to retreat and capitulate. There is yet no detectible "soft under-belly," to employ a Churchillian characterization, apparent in the armor-plate of any of these disorders. Campaigns, military and other, have to be fought with available tools and ammunition. While we await the development of scientific tools which can carry the battle to the innermost sancta of the redoubts of these well entrenched enemies there must be no let-up in the scientific attack upon a host of other diseases with more overt evidences of cracks in their topography.

Medicine — An International Language

There are no areas of confidential information in medicine. An important discovery made on one continent is editorialized by medical journals everywhere and quickly becomes the property of all the peoples of the

Continued

world. The late President, John F. Kennedy, spoke of this international aspect of science in addressing the Centenary of the National Academy of Science just a month before his tragic death. "The great scientific challenges," he said, "transcend national frontiers and national prejudices. . . . The language of science has always been universal . . . but the contemporary revolution in transport and communications has dramatically contributed to the internationalization of science . . . and the increase in organized international cooperation." Medicine, more than any other activity or discipline, makes the whole world kin. When the quality of sympathy and community of feeling, at the basis of all good medicine, enter more freely into all human enterprises, the problems of food and shelter for all and of education for our children will loom less formidable and unremediable than they now appear in many parts of the world. Society and medicine together are working unrelentingly to set aside the dictum of natural selection by the survival of the fittest. Society is no longer content to leave the straggler and the handicapped to their own fate. With medicine as a strong ally, a large proportion of such persons today can be salvaged for lives of usefulness and personal fulfillment.

War, Pestilence, and Disease

Throughout the ages, war and pestilence have been the chief levelers of population growth. Medicine and society have succeeded in eliminating many of the plagues which, through the centuries, have decimated peoples in all areas of the world. Yet struggles for advantage continue unabated.

The final lessons of most wars have been their utter futility. There were eight million battle casualties amongst all combatants in World War I; 10 million in World War II; in addition, approximately 15,000,000 civilians were killed by massacre, starvation, ill treatment, disease, and bombing.[16] More than two thirds of the nine million Jews in Europe were annihilated, an outrage to the dignity and humanity of man which must plague the conscience of all for centuries to come.

The horror and holocaust of war should persuade the peoples everywhere to learn to resolve their differences, with advantages for all. Many here this evening know of the deprivation suffered during the German occupation by surgical friends in Holland, Denmark, and Norway. At war's end, some of them affected not to understand when addressed in German. Mrs. Wangensteen and I were privileged to attend the German Surgical Congress in Munich a year ago. Its President, Rudolf Nissen, distinguished Professor of Surgery at Basel, had been exiled by Hitler from his position in Berlin at the beginning of hostilities in World War II. At an informal gathering for foreign guests of the Congress, the well-known Danish surgeon, Erik Husfeldt, leader of the Underground Resistance Movement in Denmark during the war, speaking in German, proposed the toast to German surgeons and surgery. Such an occasion indicates that man is willing and able to overlook and forget his worst hurts, once etched deeply on his memory. The passion of resentment, if constantly rekindled, only consumes. If all man's efforts were directed at improving our common lot, what a different place this world could be!

Surgery's Dependence Upon Other Disciplines

In writing of his earlier training days in Berlin (1835-40), Jacob Henle (1882) said important discoveries could be "achieved by scratching a membrane with the nail or a scalpel." The British anatomist, Sir Robert Christison, likened Anatomy to a harvest field. "First come the reapers," said Christison, "who enter upon untrodden ground and cut down great stores of corn from all sides," amongst which group he listed Vesalius, Fallopius, Malpighi, and Harvey. "Then come the gleaners, who gather up ears enough from the bare ridges to make a few loaves of bread," in which group he mentioned Valsalva, Haller, Winslow, Hunter, and others. "Last of all," said Christison, "come the geese, who still contrive to pick up a few grains scattered here and there among the stubble, and waddle home in the evening, poor things, cackling with joy because of their success."[17] "We are the geese," added Christison. Osler (1894) very properly noted that such unrewarding gleaning comes from protracted searches in a restricted field.[18]

Claude Bernard said, "Medicine is not a science; it is a combination of sciences." Every important development in medicine serves to emphasize the importance of Bernard's observation. Empiricism, the experience and technical skills of surgeons, pharmacy, chemistry, experimental pathology, microbiology, and pharmacology, all play significant roles in the development of antiseptic and aseptic surgery, an interesting story too long for narration here.

Research

Since World War II, people everywhere have become deeply interested in many facets of research and their social implications. In consequence medicine is dealing with a continuously better informed public, which is as anxious to know that research is liberally supported as it is to learn the fruits of research. Several years ago, the husband of a former patient brought a friend of his to see me. The three of us chatted amicably in my office for some twenty minutes. Finally the visitor said to his (and my) friend, "Why are we here?" My friend replied, "We are here to talk about your problem." The visitor answered, "I have no problem." Retorted my friend, "Yes, you have." Inquired the visitor, "Well, what is my problem?" Said my friend, "It is your money; your money is your problem."

The upshot of this was that my patient called me later that afternoon to indicate his friend was contributing $100,000 to our research funds, which over the years have now grown to $300,000. About ten days after the first gift, however, my generous donor called to inquire, "Well, what have you discovered?" As all learn, who work hard at the pleasant but arduous game of research, and benefactors too, rewards are not gathered so quickly.

During my wanderjahr on the European Continent almost 40 years ago, I remember well a visit to the Kaiser-Wilhelm Research Institute, just outside of Berlin. Like a penniless little boy looking through a bakery window at delectables, I could only wish we could some day be fortunate enough to have in our country a research institute of this quality and magnitude. World War II succeeded very definitely in persuading our government, as well as our people, that research in all areas, including medicine, pays off handsomely. Current annual appropriations by our Congress for medical research are now in the area of a billion dollars.

In the midst of the depression years (1930-1939), world famous Surgeon William Mayo, of whom every Minnesotan is proud, and who for 32 years was a distinguished Regent of the University of Minnesota, persuaded the Legislature to provide the University's Medical School with an annual budget of $50,000 for research. To us at the time, it was like manna from Heaven, though more than 50 individuals shared in partition of the monies. Today, several investigators in our school receive more than $100,000 each for support of their own research. The largesse of our government has been magnificent; but in the end, it is the great interest, faith, and confidence of the public in research that makes all this possible.

In 1957, I was privileged to participate in a discussion on medical education at the University of Melbourne. No one having mentioned research, I thought it timely to bring it into the discussion, to which suggestion, a well-known surgeon in the area retorted, "Oh, that God-awful word!"

Even in certain circles closer to home, one hears said today, "There is too much research." "Give the medical school back to the students." "Researchers are a dime a dozen." These philosophies, however well intended, distort the situation badly. The contrary is certainly true. Only in an atmosphere of advancing knowledge is the student stimulated to do his very best. "Research, research, and more research," is the stirring admonition of that wise clinician, Paul Dudley White,[19] known to physicians everywhere.

We who are fortunate enough to enjoy the opportunities for research must take care not to assign these privileges second or third places in our thoughts. We must not be unmindful that experimental laboratories

Continued

for medical schools are essentially a product of this century.

The Doctor's Consulting Room

Prior to the cinema, radio, and television, the elementary school pupil was usually home evenings, hovering about a table in the family parlor near a small central source of light. Whatever defect the arrangement provided, it did afford the opportunity for the youngster to acquire a love of reading, emphasized by Anthony Trollope (1815-1882)[20] in this delightful admonition to college students: "With reference to the habit of reading, I make bold to tell you it is your pass to the greatest, the purest, and the most perfect pleasures that God has prepared for his creatures. Other pleasures may be more ecstatic. When a young man looks into a girl's eye for love, and finds it there, nothing may afford him greater joy for the moment: when a father sees a son return after a long absence, it may be a great pleasure for the moment: but the habit of reading is the only enjoyment I know, in which there is no alloy. It lasts when all other pleasures fade, it will be there to support you when all other recreations are gone."

The medical library is the doctor's consulting room. It is there physicians and investigators acquaint themselves with developments in the area of their own interest.

It is a thrilling and rewarding experience to enjoy the wonderful privilege of studying in the presence of great books, whose pages preserve the permanent and immortal legacy of great ideas. Many a student in the many disciplines of medicine who avail themselves of this privilege find their sights lifted and the nature of their dedication increased by contact with the inspiring stimulus of a fine library. Its atmosphere works silently upon the mind, uplifting the spirit and enlarging the student's vision, not unlike the stirring urge of the Divine.

When John Shaw Billings[21] made his famous address on our medical literature at the International Medical Congress held in London in 1881, he said: "There are 180,000 medical men scattered through the world, of which 65,000 are in the United States." Today the Director of the World Health Organization and the World Directory of Medical Schools[22] (1963) indicates there are 1,513,147 physicians in the world, of which number 234,294 are in the United States. There are today, therefore, more physicians in the United States than there were in the entire World in 1881. Billings added that for the calendar year 1879, the Index Medicus Catalogue of the Surgeon General's Office listed 1,643 books published throughout the world, of which 310 originated in the United States. There were 635 current journals on the shelves of the Army Medical Library (now the National Library of Medicine), when Billings reported upon his Survey in 1881. Today there are well in excess of 6,000 current medical periodicals, and most libraries like our own carry on their shelves at least 1,500 current numbers. Altogether in the biomedical field there are almost 9,000 medical serials.[23] It is quite obvious, therefore, that the medical sciences too have parallelled the population explosion in publication, all of which serves to point up the clinician's dilemma in trying to keep abreast of developments in his own field.

The brilliant German physiologist, DuBois Reymond,[24] more than 80 years ago emphasized the importance of historical approach to all studies, whether they concerned organizations, politics, language, or the sciences. The famous French medical historian, Emile Littre,[25] had some years previously pointed out that medicine must occupy itself with its history and develop a spirit of caring for monuments inherited from the past. Study of the history of medical disciplines provides scientists with an orientation they cannot otherwise acquire. Study of medical history enlarges the investigator's knowledge, broadens and strengthens his judgment, providing him with rich mines of the neglected. It also stimulates a respect and veneration for ideals and in the truest sense makes for better doctors. With the constant acceleration of the growth of knowledge, it is important that we not abandon the study of the lessons of the past. A study of medical history teaches the prospective doctor as well as the investigator how to separate wheat from chaff, while attaching humanistic values to the instruction.

A study of medical history is not to be thought of as delightful pastime for those contemplating the disengagement of retirement. Historical analysis is a most useful device in bringing into sharper focus the thoughts, considerations and theories which have advanced or retarded medical progress. You will be pleased to know that the medical school will presently establish a department of medical history which will add an important ingredient to the atmosphere of our school. As most of you are also aware, the medical school with a modest legislative appropriation and with important help from loyal friends in the community, is bringing to fruition a great medical library. I would like to believe that in the foreseeable future the medical profession of Hennepin and Ramsey Counties might come to enjoy its opportunities and privileges. Perhaps an appeal to the proper authorities might even overcome the current hurdle of available parking space!

The Surgeon and his Image

Every man needs to reassess his image periodically to note where he has been and where he is going. The minister of the Norwegian Lutheran Church in a small village in Becker County where I was confirmed as a boy 52 years ago, chose as his text of admonition to the confirmation class the well-known advice from Jeremiah: "Thus saith the Lord, Stand ye in the ways, and see, and ask for the old paths, where is the good way, and walk therein, and ye shall find rest for your soul." It is indeed sage advice. If a young surgeon knew exactly what he would like to make of his life, he might be well advised to repose judgment of how to arrive at such a goal in the hands of a competent person who could provide the needed counsel. I have known young surgeons who believe they can cultivate a large private practice and pursue simultaneously an academic career in research. Unfortunately either one of these areas is so demanding in time and energy expenditure that it takes all the strength and time anyone of us has to achieve in either domain. Life is a competitive process from beginning to end. The story of the race between the turtle and the hare certainly was no fable! During the intervening years I have thought many times of our minister's sober advice concerning stock-taking, but sadly, not often enough. One lives both by the calendar and by the clock. Perhaps one of the most important decisions anyone has to make is how to partition his time. Every man's foremost desire in life is to find that work which will prove soul-satisfying. It is the tyranny of the urgent present that robs many of us of our effectiveness. There are so many things to do; some we *have* to do; others we *want* to do; and not enough time in which to do them all.

Young surgeons, I know from experience, would rather operate than eat. As a group, they are men of action. Many academically oriented surgeons, believing themselves younger than the calendar suggests, continue spending most of their waking hours operating, thus often stifling their own laudable aspirations.

Though obvious evidences of operative skill characterize the accomplished surgeon, it must be recognized there are more important determinants for progress in surgery. Whereas there are those who say the most strenuous work the surgeon does is scrubbing his hands, in preparation to operate, yet anyone who has stood at the operating table for long hours knows what the toll is, not only in physical fatigue, but in mental acuity too. Whereas many a young surgeon may feel by continued application he will become a Paderewski or a Fritz Kreisler with the scalpel, there is more to surgery than this. The well balanced surgeon, conditioned to withstand physical and emotional strain, encompasses a large fund of factual knowledge with judgment and wisdom learned from experience, in addition to operative skill. My experience as a teacher suggests that of these qualities so important for the surgeon, operative skill, granted reasonable neuromuscular control, is probably most easily acquired. It has always been a source of continuing wonder to me to observe how quickly operative skills are acquired by young surgeons. Those who profess a desire to

Continued

continue the arduous climb up the academic ladder are ill advised to spend most of their waking hours in the operating room. Care must be taken not to become completely engulfed by the many magnetic and accessible attractions of the surgeon's life, including large pecuniary rewards. A more even allocation among study, research, teaching and thinking about problems of the craft is important and desirable, as they are all important components embraced in the minister's advice of frequent assessment of the direction in which anyone of us wants to go.

King James I,[26] of England, said: "I can make a Lord, but only the Almighty can make a gentleman." No man in his hurry to reach his goals can afford to neglect his associates, upon whom we are all very much dependent for counsel and criticism. An occasional critical look at oneself in the status-mirror of life advised by the Old Testament Prophet, can be of great benefit to all.

Thinking is some of the hardest work we have to do. It is probably far easier to go to the operating room and do another operation or two or to the library and consult another dozen or even a hundred more references. The state of diminishing returns is not solely a guideline for economists.

Changing Attitudes of Practice

With the prospect of control of infectious diseases almost in sight, need to accelerate global studies of population control is becoming increasingly evident. At the present rate of growth, the United States is doubling its population every 40 years, and by the year 2000 will be a country of 350,000,000 people. A few areas in the world are doubling population at considerably shorter intervals. Despite our increased capacity to produce food, the time will most certainly come when the world will be overpopulated unless interplanetary travel opens up new avenues for colonization or export.

Since 1880, there has been a four-fold increase in our population (U. S.) while our present physician increase has been only 3.6 times that of 1880. The public continues to clamor for more doctors, an ever increasing number of whom are going into specialties. The tremendous gains in medical knowledge through the agency of research will continue to attract larger number into research areas and specialty practice. The care of many types of illness today is essentially the responsibility of a specialist and the growth of specialism in Minnesota, as well as throughout our land, has been astounding since the end of World War II, and will undoubtedly continue because of medicine's increasing complexity. Trends toward more general adoption of the clinic idea, to which the Brothers Mayo lent such significant impetus, might well become the standard condition of practice everywhere in our country. Thoughtful integration of general practitioners and specialists into such clinic practice would provide all concerned with more satisfying conditions of work, appreciated by all as very important components of emolument. Such practices too would probably find favor with the public.*

Growth of Blue Cross and other insurance plans affect very materially the economic class of patients coming to university clinics throughout our country. Up until the beginning of World War II, there were in fact very few private patients in our wards. World War II changed all this. Most medical schools and ours too, under the leadership of Dean Howard, have made important strides in establishing controls which serve to remind the full time university clinician that his primary objective is not to cultivate a large private practice, which endeavor, if successful, would only succeed in stifling his professional growth.

Importance of Universities

With wise guidance from a number of medical school deans and university presidents, and with generous support from the profession and the people of Minnesota speaking through its legislative body over a period of more than four decades, increased stature has been and continues to be added to our School. If the University of Minnesota and its Medical School are to continue to hold their position and prestige in the intellectual and professional world, they will continue to need the whole-hearted support of this medical community. Some of you will remember the immortal words of the Poet Laureate John Masefield (1946) of England, who said: "There are few things more enduring than a university. Religions may split into sects or heresies; dynasties may perish or be supplanted, but for century after century, the university will continue, and a stream of life will pass through it, and the thinker and the seeker will be bound together in the undying cause of bringing thought into the world."[27] Liberal support of our schools, universities, and professional colleges by the public is a sound and probably the wisest investment for a bright and glorious future for any country.

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*An interesting monograph entitled Planning for Medical Progress Through Education sponsored by the Association of American Medical Colleges has just appeared in print. This report may come to have as great an impact upon medical education as the Flexner Report of 1910. It stresses the team approach to medical problems, a thesis which this writer has espoused for many years (J Lancet 70:73, 1950).

The Computer — Not the Final Answer

The complicated structure of medicine which came into being as a consequence of the providential scientific period of fecundity of the post-war period served to emphasize the importance of research, which only in the second quarter of the present century has come to be fully appreciated. Today almost every hospital in a metropolitan medical school area desires an affiliation with the school, knowing that the fruits of research are reflected directly through all the activities of the Hospital, an impact that comes to be appreciated and felt by its board of trustees as well as by its patrons, the public.

Where the new scientific innovations will take us only the future and its experience will determine. Certain it is we shall continue to have more science and less empiricism in medicine, but in the age of the computer, competence, experience and dedicated devotion to his tasks are still the hallmark qualities of heart and mind of the good doctor and are so much appreciated by the sick. Sympathy, which is not to be found in a computer, continues to be the best solvent for the ills of man. William MacLure, beloved Doctor of Drumtochty, immortalized by Ian MacLaren in the Doctor of the Old School, is not a forgotten legend.[28] Medicine and love of one's fellow man are inseparable. A selfless devotion to his patients is still the guiding precept of a large segment of our profession here and everywhere. The late Carl Eggers, a New York thoracic surgeon, well-known to many surgeons here, paid a visit to his native Oldenburg shortly before his death and was asked to inscribe his name on the city's official ledger. After a moment's reflection, he wrote, "It is so easy to do good in the world and it makes one so happy."[29] Such is daily the great privilege of all of us and particularly so in medicine.

The late Walter B. Cannon,[30] who spent much of his childhood in St. Paul, relates in his autobiography, The Way of any Investigator, that his dying mother called him to her when he was ten years of age and said, "Walter, be good to the world." That the obedient son listened attentively and responded in a manner honoring medicine's finest traditions and with important benefits to medicine and mankind, every physician knows. I have the feeling that in the years ahead, with thoughtful evaluation of life's real satisfactions and rewards, we shall see a renewal of interest in and increasing evidences of an anxiety of our profession to improve our public image.

The future of medicine and surgery demands that while we strive to improve the science of our craft, we do not neglect the compassionate graces of sympathy, mercy and charity.

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6-30 May be obtained from the author or the reprints.

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Maternal Mortality Studies

Maternal Mortality in Minnesota Due to Anesthesia*

Anesthesia continues to account for a significant proportion of the deaths in Minnesota due to obstetric causes. Sixteen such deaths occurred in the first 12 years of the state-wide Minnesota Maternal Mortality Study extending from 1950 to 1962, accounting for 5% of all deaths due to obstetric causes and for 9% of those considered preventable. Eleven of these 16 deaths were considered preventable. Among all causes of death, only hemorrhage, toxemia, and infection accounted for more fatalities in the preventable category.

It is of interest to note that death certificate information indicated anesthesia as the primary cause of death in only four cases. In the others anesthesia became evident as the cause only after the circumstances involved were investigated and the case considered by the Minnesota Maternal Mortality Committee.

A survey conducted in Minnesota by Knudsen, Rosenfield, and Lundgaard has shown that personnel adequately trained for administration or supervision of obstetric anesthesia is all too frequently not available. Of 174 hospitals offering obstetric services in the state, only 11 provided obstetric anesthesia supervised by anesthesiologists. One hundred four hospitals employed registered nurses, primarily on general duty, to give routine obstetric anesthetics.[1] This neglect is made evident by the results of this study which show that tragedies have occurred through errors made in large part because of inadequate training on the part of those responsible. In general, the choice of anesthetic was frequently wrong, the dosage administered was excessive, the patient was poorly prepared and inadequately supported, and resuscitative measures were delayed and inadequate. In none of the cases was the anesthesia supervised by an anesthesiologist. In two anesthesia was administered by untrained nurses, and in a third by a student nurse-anesthetist. Six were administered by registered nurse-anesthetists, one general anesthetic by an untrained physician, and the four spinal anesthetics and two regional blocks by the surgeon-obstetrician in each case (Table 1).

TABLE I
Obstetric Anesthesia Deaths in Minnesota, Type of Death, and Personnel Administering Anesthetic

		Anesthetist		
Type of Death	No.	Physician	R.N.A.	R.N.
Spinal	4	4		
Regional Block	2	2		
Aspiration	6		4	2
Hypoxia	4	1	2	1
Totals	16	7	6	3

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*From the Minnesota Maternal Mortality Committee.

Address for reprints: St. Louis Park Medical Center, 4959 Excelsior Boulevard, Minneapolis, Minnesota 55416.

Continued

While the study shows that the anesthetic was generally poorly chosen or poorly given, it is also clear that the death was frequently the end result of failure to follow basic principles of adequate patient work-up and conservative obstetric practices. Death from anesthesia was merely the culminating catastrophe that followed gross errors in management. For example, of six Cesarean sections performed, two were considered not indicated by the committee, and a third was a repeat section in a patient in whom the original section was not indicated. Of the other operative procedures performed approximately one half were either unindicated or were forceps procedures prematurely applied. In several instances obstructed labor was unanticipated because of inadequate pelvic evaluation, and in another case severe anemia was neglected, the patient dying of hypoxia when general anesthesia was applied by an untrained person.

The 16 fatalities included four from spinal anesthesia, two from regional block anesthesia, and six associated with aspiration; in four cases the principal precipitating cause of death was hypoxia.

Spinal Anesthesia

The principal problem in this group was the failure to appreciate the intolerance of pregnant patients for ordinary doses of anesthetic agents administered intrathecally. In all cases the dose of the anesthetic was excessive, varying from 120 mg. of procaine to 20 mg. of pontocaine, when maximum safe doses for the pregnant woman are considered to be 75 mg. and 8 mg. of each respectively. The Trendelenburg position was sometimes used, thus adding to the problem by increasing the height of the anesthetic level. Furthermore, in all cases there was complete neglect of provisions for checking anesthesia level, and measures for combatting vascular collapse and respiratory paralysis were lacking. It is most encouraging to note, however, that there have been no deaths from spinal anesthesia in obstetrics in the state since 1952.

Case Reports

Case #1

This patient was a 35-year-old para 7-0-0-7, for whom delivery by Cesarean section was planned because of previous section. She was anesthetized while in early labor with 120 mg. of procaine administered intrathecally and was given 2½ mg. of neosynephrine intramuscularly at the time of the application of the spinal, which was done by the surgeon. The patient was tipped in slight Trendelenburg position. No fluids were administered. No blood pressure determinations were done, and no check of the anesthesia level was made. A classical Cesarean section was performed with delivery of a normal 6½-pound infant. As the uterine wound was being closed the patient became gray, her pulse became impalpable, and she ceased breathing 20 minutes after application of the anesthesia. Blood loss had been minimal.

Case #2

The patient was a para 1-0-0-1 who was delivered of her first pregnancy by Cesarean section because of "outlet contraction." No record of pelvic measurements could be found. Cesarean section was carried out at 37 weeks' gestation with the anesthesia consisting of 20 mg. of pontocaine in 3 ml. of dextrose solution. As the skin scar was being excised, the patient became pale and then cyanotic. Respirations became very shallow and the pulse weak and thready. Twenty minutes after injection of the anesthetic, respirations ceased and the patient expired, despite application of artificial respiration and the administration of oxygen, coramine, and adrenalin.

Case #3

A 29-year-old primigravida requested that she be delivered by Cesarean section.

Because of this and because of a breech presentation, the physician agreed, although he considered the pelvic measurements normal. Anesthesia was produced by the injection of 18 mg. of pontocaine in 4 ml. of spinal fluid. The patient was kept flat for 10 minutes and then tipped in moderate Trendelenburg position. As the skin incision was being made the patient's blood pressure disappeared, and respirations ceased 15 minutes after the injection of the anesthetic. A rapid section was done and a living baby delivered, but efforts to resuscitate the mother failed.

Case #4

This patient was a 38-year-old para 6-0-1-6 whose course was complicated by hypertensive cardiovascular disease with superimposed toxemia. At 27 weeks' gestation she developed gross edema, blood pressure of 220/140, choked discs, and oliguria with 3+ albuminuria. Cesarean section was decided upon and anesthesia produced by injection of 150 mg. of procaine intrathecally. Almost immediately after application of the anesthesia her blood pressure was 60/0. She was given ½ ml. of adrenalin and 1 ml. of coramine, and terminally a blood transfusion was begun. Treatment failed and the patient was pronounced dead 30 minutes after injection of the procaine.

Regional Block Anesthesia

Both deaths in this category followed the performance of paracervical and pudendal blocks during labor in normal multiparous women. Each death occurred primarily as a result of the injection of toxic amounts of the anesthetic drug — 400 mg. of Cyclaine in one case and 1000 mg. of Xylocaine in the other — into a very vascular area. Resuscitative measures in both cases were somewhat delayed and inadequate.

The possibility of inadvertent intravascular injection must be borne in mind and guarded against in performing these blocks. It should also be pointed out that it is now known that an adequate volume consists of 7 or 8 ml. on either side for the paracervical and 5 ml. on each side for pudendal blocks done transvaginally. The current drugs of choice are Xylocaine, Carbocaine, or procaine in a 1% concentration.

Case #5

The patient was a 32-year-old para 1-0-0-1 who began labor spontaneously at 38 weeks' gestation after a normal prenatal course. After 3½ hours of uneventful labor, bilateral paracervical block was done with 10 ml. of 1% Cyclaine on each side, together with bilateral pudendal block with the same dosage. The total amount of the anesthetic injected was 40 ml. At this time the cervix was 7 cm. dilated, the patient's blood pressure was 128/76, and her general condition was good. Less than 15 minutes later she developed a generalized convulsive seizure and became cyanotic. Treatment consisted of oxygen and 5 ml. of sodium pentothal of unknown concentration injected intravenously. After two more convulsive seizures her blood pressure became unobtainable. Meanwhile delivery was accomplished by outlet forceps extraction. Despite administration of adrenalin, artificial respiration, and 2 grains of sodium amytal intravenously, the patient expired 25 minutes after injection of the anesthetic. Autopsy showed no anatomic cause of death.

Case #6

This patient was a 26-year-old para 1-2-0-2 who was admitted to a hospital at 25 weeks' gestation. The cervix was partially dilated and the patient was having irregular contractions. After 40 hours a Shirodkar procedure was carried out under spinal anesthesia produced by 50 mg. of Cyclaine. However, the patient went into active labor and delivered 3½ hours after surgery. Pudendal and paracervical blocks were carried out, using a total of 100 ml. of 1% Xylocaine. Ten minutes after delivery the patient developed generalized convulsive seizures and vasomotor collapse and lost consciousness. The convulsions were controlled after two hours with sodium pentothal anesthesia, but administration of blood, intravenous fluids with vasopressors, and oxygen failed to correct the vasomotor collapse. The patient died nine hours post partum. Autopsy was negative except for some evidence of intrauterine and urinary tract infections.

Deaths Due to Aspiration

The six deaths associated with aspiration illustrate a number of points.

Continued

Three resulted from mechanical obstruction of the trachea and/or bronchi while three resulted from overwhelming pulmonary edema due to aspiration of liquid gastric contents as described by Mendelson.[2] These deaths show that oral intake of liquids as well as solids during labor can be dangerous if general anesthesia should subsequently be required.

Treatment of the effects of aspiration is unsatisfactory. Administration of oxygen under positive pressure and the use of steroids have been advocated, but in many cases neither is adequate. It has also been shown that bronchoscopy is frequently of little help, particularly after aspiration of liquid stomach contents.

The best "treatment" is clearly preventive. It is essential that food and fluids be withheld during labor if there is a possible need for subsequent general anesthesia. It should be borne in mind that gastric emptying time may be indefinitely prolonged during labor. If operative delivery becomes necessary despite the fact that the patient is known to have liquid or solid food in her stomach, some form of conduction anesthesia should be used. Vomiting can still occur but, if the patient is awake with intact reflexes, significant aspiration will not occur. If there is no alternative to general anesthesia, intubation of the trachea should be carried out preoperatively by someone experienced with this technique. It has been shown, however, that even intubation can be dangerous, as instances of vomiting and fatal aspiration under the anesthesia given for the purpose of intubation have been reported.

This group again illustrates instances of poor selection of anesthetic agents (nitrous oxide for a midforceps extraction, for example), poor technique with inadequate depth of anesthesia before operative manipulations were begun, and inadequate patient support and resuscitation. Many gross errors in obstetric management are also apparent. One death resulted from the administration of trichlorethylene by a nurse. This agent is meant to be used only for analgesia and to be self-administered by the patient.

Case #7

This patient was a 36-year-old primigravida with an incompletely measured pelvis. She was five feet tall and weighed 250 pounds. Spontaneous onset of labor occurred at 42 weeks' gestation. During a prolonged desultory labor of 40 hours duration, the fetal heart tones disappeared. Three hours later the cervix was completely dilated, and the fetal head was at the level of the ischial spines in the right occipitotransverse position. A decision was made three hours later to deliver the patient by midforceps extraction, and she was anesthetized with nitrous oxide by a nurse-anesthetist. As the forceps were being applied, the patient developed laryngeal spasm and became deeply cyanotic. An unsuccessful attempt was made to insert an airway. Administration of oxygen by bag pressure failed because of the laryngeal spasm. The patient vomited, developed generalized convulsive seizures, and expired 20 minutes after the beginning of the attempted forceps delivery. Up to five hours before delivery, the patient had been given liberal amounts of fluid orally.

Case #8

The patient was a 22-year-old primigravida who was known by x-ray pelvimetry to have borderline measurements both at the inlet and mid-pelvis. Because of this, labor was induced with intravenous oxytocin at 38 weeks' gestation. After a six-hour first stage of labor, progress ceased. After four hours of second-stage labor an attempted midforceps rotation and extraction under ether anesthesia failed. During this process the patient vomited. Cesarean section was then carried out under pentothal anesthesia administered by a nurse-anesthetist. Prior to administration of the anesthetic the patient was coughing, and during the procedure she vomited and aspirated liquid bile-stained material. The trachea was aspirated with a catheter, but the patient remained cyanotic. At the conclusion of the operative procedure, she was cyanotic with a pulse rate of 160, respirations of 45, and physical evidence of consolidation in both lungs. She then developed peripheral vascular collapse and died four hours post partum. Autopsy showed marked bilateral hemorrhagic pulmonary edema.

Case #9

This patient was a 28-year-old para O who went into labor spontaneously at term. The first stage of labor was some 34 hours in duration and was characterized by administration of excessive medication for sedation and inadequate treatment for uterine inertia. The patient had frequent emeses and was fed regularly. She was seen in consultation by an obstetrician who found the cervix to be completely dilated with the head at station plus 1 in the right occipitotransverse position. On his instructions the patient was anesthetized by a nurse-anesthetist with 50% cyclopropane for one minute, followed by 30% with a gradual change over to ether. After six or seven breaths of ether, forceps application was made and an attempted rotation was carried out. The patient promptly vomited. She was inadequately suctioned and no intubation was done. She was re-anesthetized and delivered. Post partum she developed fever of 103°, cyanosis, blood pressure of 90/50, pulse rate of 160, and respiratory rate of 50. Physical examination and chest x-ray showed evidence of pulmonary edema and atelectasis. Despite digitalization and treatment with antibiotics, hydrocortisone, and oxygen, the patient died with continuing respiratory difficulty 44 hours after delivery.

Case #10

This patient was a 21-year-old para 0-1-0-0. No adequate pelvic evaluation was done, although simple flat films of the pelvis were taken, which indicated probable inlet and mid-pelvic contractions. The patient went into labor at term with the fetal head floating. After 24 hours of hard labor the cervix was completely dilated, and an attempt at high forceps extraction was made under ethylene anesthesia. The delivery attempt failed, and in the process the fetal heart tones disappeared. The patient was allowed to recover from the anesthesia, after which she was given oral fluids. After 6½ hours of second stage and a total labor of 31 hours, a difficult midforceps extraction of a stillborn infant was done under ethylene anesthesia of 30 minutes' duration. The anesthesia was given by a student nurse-anesthetist. During delivery the patient vomited twice, and following the second episode she remained cyanotic despite administration of oxygen and aspiration of the mouth and the pharynx. Her blood pressure after delivery was 80/0. She remained cyanotic and in shock. Evidence of pulmonary edema appeared, and death occurred four hours after delivery.

Case #11

A 29-year-old para O was subjected to laparotomy for an ectopic pregnancy under pentothal-curare anesthesia administered by a nurse-anesthetist. Laparotomy was begun three hours after the patient had consumed some soup and tea. When the abdomen was being closed, it was noted that the patient was not breathing, and she promptly died despite efforts at resuscitation. There was no evidence of vomitus in the mouth or pharynx, but autopsy showed the bronchi and trachea to be filled with thick mucoid material containing numerous food particles.

Case #12

This patient was an 18-year-old para O who was admitted to the hospital in early labor at term. Four and one-half hours after admission the cervix was thought to be completely dilated, and she was moved to the delivery room where trichlorethylene was administered with contractions by a nurse untrained in anesthesia. This was continued for an hour and 45 minutes with a Duke inhalator set at "a little past 5." The patient then appeared to be under deep anesthesia. Contractions ceased and she retched several times. She then became cyanotic, had several generalized convulsions and died in about 10 minutes. At autopsy the trachea and bronchi contained aspirated stomach contents, and there was complete atelectasis of much of both lungs. It was known that the patient had not taken any solid food for more than 12 hours before delivery, but the records did not indicate whether she had been given liquids.

Deaths Due to Hypoxia

In each of these cases the patient was in poor preoperative condition for general anesthesia. Complications included anemia, hypovolemia, and restriction of respirations due to previous chest surgery or obesity. In general the choice of anesthetic was poor and it was poorly administered. It is known that patients with restricted alveolar ventilation are prone to

Continued

the development of respiratory acidosis. Pentothal and curare, which were used in three of the four cases, may further depress respirations, and a vicious cycle develops from which the patient cannot be recovered. The anesthetic risk in these patients is particularly high, and expert handling is essential.

Case #13

This patient was a 21-year-old para 2-0-0-2 whose prenatal course was complicated by toxemia and anemia. On admission to the hospital her hemoglobin was found to be 6.9 grams per 100 ml. The anemia was not treated. Spontaneous onset of labor occurred, and the first of a set of twins was delivered after 2½ hours of labor. Despite stimulation with pituitrin the second twin was not delivered until 15 hours later. The placenta was then retained and after two hours manual removal was attempted under open drop ether anesthesia administered by a nurse who had no anesthesia training. As the operative procedure was being completed the patient stopped breathing. Manual artificial respiration was done, oxygen was administered, and terminally whole blood was pumped in; but there was no response and the patient was pronounced dead one-half hour later.

Case #14

This patient was a 42-year-old para 0-0-2-0 who had a 15-year history of treatment for pulmonary tuberculosis, including oleothorax. She had a marked reduction of pulmonary function with a vital capacity of 1200 ml., plus electrocardiographic and physical evidence of right ventricular strain and hypertrophy. After she had developed signs and symptoms consistent with a diagnosis of early ectopic pregnancy, exploratory laparotomy was planned. She was anesthetized by a nurse-anesthetist with pentothal-curare and promptly became cyanotic. Intubation was carried out and the patient was given some isuprel intravenously. Bag breathing was instituted, but within 15 minutes the blood pressure had dropped to 80/54. Despite administration of blood, 2 ml. of Tensilon and atropine intravenously, the patient died an hour and 20 minutes after the anesthesia was begun. No surgery was performed. Autopsy showed an ectopic pregnancy involving the left tube and dilatation and hypertrophy of the right ventricle. The trachea and bronchi were clear.

Case #15

This patient was a 28-year-old para 2-0-0-2. Classical Cesarean section was carried out at 41 weeks' gestation without indication. The patient had been having false labor for a week and was edematous, but the findings were otherwise normal. Premedication consisted of 50 mg. of demerol and grains 1/150 of atropine intravenously. The anesthesia as administered by a physician who had no anesthesia training and consisted of 2½% pentothal with curare and nitrous oxide-oxygen in a 2-1 mixture. The duration of anesthesia was one hour. Immediately after the surgery was completed respiratory failure developed. Following this the patient remained cyanotic with a pulse rate of 130 to 160 and blood pressure of 170/100. She was given oxygen and two doses of Tensilon of 1 ml. each intravenously. One hour post partum her blood pressure fell to 80/60. She vomited several times and developed convulsive movements and restlessness. She died in respiratory failure nine hours post partum.

Case #16

This patient was a 44-year-old para 7-0-3-6. She was very obese with a weight of 210 pounds and a height of four feet, nine inches. She was also hypertensive. At 24 weeks' gestation she developed strangulation in an incisional hernia. Surgery was carried out for reduction of the hernia under sodium pentothal anesthesia administered by a nurse-anesthetist. Immediately after the administration of the pentothal the patient became cyanotic and remained so despite intubation and artificial respiration with a bag. The surgical procedure was one hour and 20 minutes in duration. The patient's color was never good, and she seemed to be "wet" despite aspiration. There was no vomiting. She was given a total of 875 mg. of pentothal and 175 units of curare. She was also given 2 ml. of Tensilon intravenously just after the surgery was begun and again just before it was finished. As the dressings were being applied, the patient's blood pressure disappeared and attempts at resuscitation were unsuccessful. Autopsy showed cardiac hypertrophy with minimal pulmonary edema and atelectasis.

Conclusions

Obstetric deaths in Minnesota due to anesthesia resulted in large part because of ineptness in the selection and/or administration of the anesthetic agents. In the majority of cases, errors in obstetric management including performance of unindicated operative procedures led to administration of anesthesia under unfavorable conditions.

Fatalities resulting from spinal anesthesia appear to be a thing of the past. The last such death occurred in 1952. Deaths from vomiting and aspiration can be further reduced by maintaining awareness of the dangers of general anesthesia in patients who do not have empty stomachs. More widespread availability of experts in anesthesia is needed, particularly for the poor risk group of patients.

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Alex Barno, M.D.
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Minneapolis, Minnesota

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Famous Preface

In his preface to the English dictionary, Samuel Johnson, 1755, stated, "I am not yet so lost in lexicogiphy as to forget words are the daughters of earth and that things are the sons of heaven. Language is the only instrument of science and words are but the signs of ideas."

In his letter to the Right Honorable Earl of Chesterfield after he had finished his dictionary, he stated, "Is not a patron, my lord, one who looks with unconcern on a man struggling for life in the water, and, when he has reached ground, encumbers him with help? The notice which you have been pleased to take of my labors, had it been early, would have been kind; but it has been delayed till I am indifferent, and cannot enjoy it; till I am solitary, and cannot impart it; till I am known, and do not want it.

"I hope it is not very cynical asperity not to confess obligations where no benefit has been received, or to be unwilling that the public should consider me as owing that to a patron, which providence has enabled me to do for myself."

Men have lost sight of distant horizons. Nobody writes for humanity, for civilization; they write for their country, their sect; to amuse their friends or annoy their enemies. — George Norman Douglas

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Attack is the reaction. I never think I have hit hard unless it rebounds.
— Samuel Johnson

Do not give dalliance too much rein. — Shakespeare

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1. Schleif, R.H.: J.A.PH.A., 46:179,1957 *U.S. Pat. No. 3,062,714

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Active peptic ulcer. Salicylates and citrates antagonize the drug's action and are contraindicated for concomitant use.

Warning
Use with caution in pregnant women.

Precautions
Keep patients under close supervision and make periodic blood counts. Use cautiously in patients sensitive to pyrazoles, in patients with histories of peptic ulcer, and in conjunction with sulfa drugs, the sulfonylurea hypoglycemic agents, and insulin, the actions of which may be potentiated.

In mobilizing urate deposits, the drug may precipitate acute attacks of gout, urolithiasis, and renal colic, especially in the initial stages of therapy. Ensure adequate fluid intake and alkalinize the urine. With renal impairment, test renal function periodically.

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The most frequent are upper gastrointestinal disturbances. The drug may activate peptic ulcer. Rash occurs infrequently. Although not reported to date, blood dyscrasias are a possibility.

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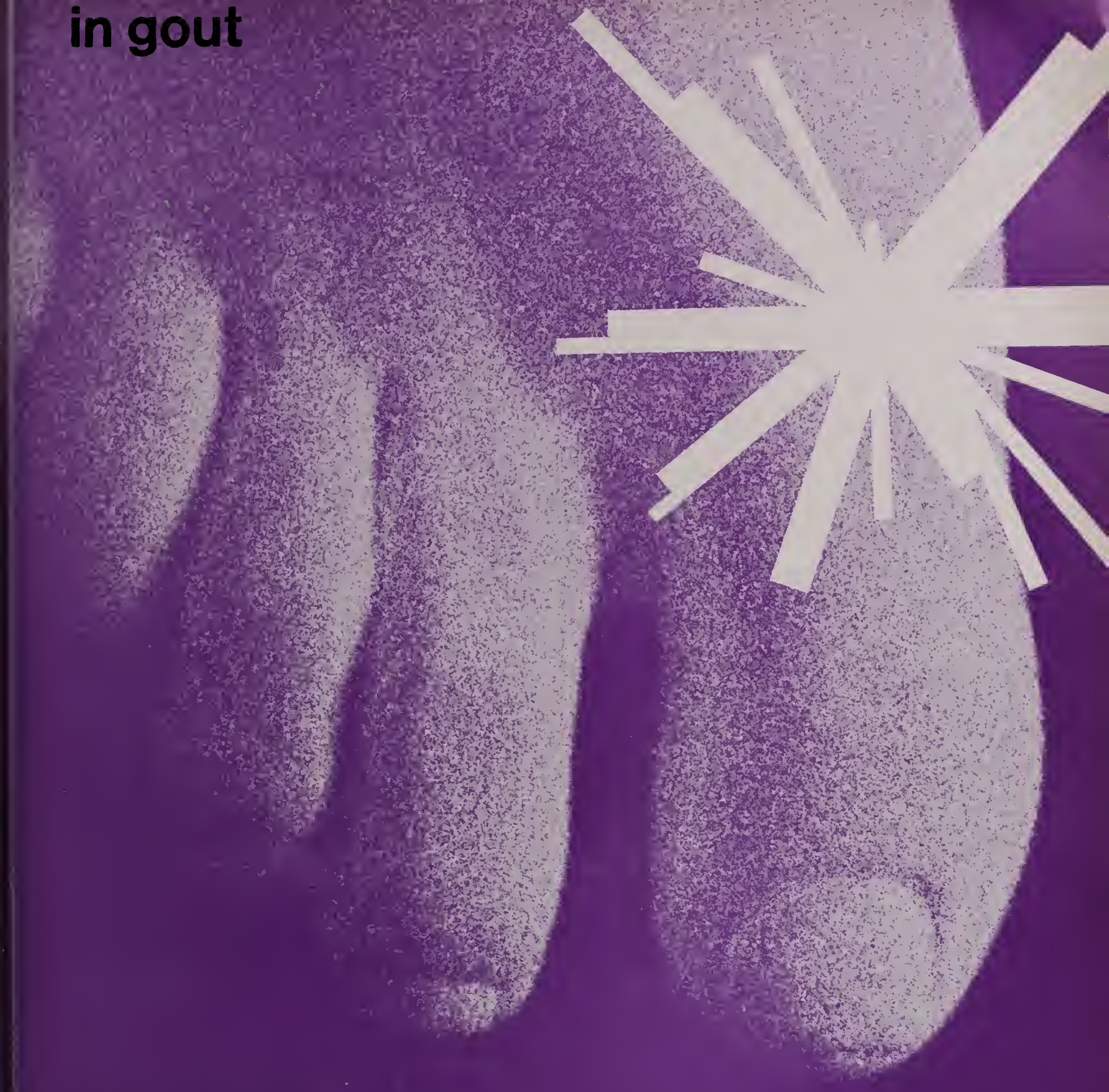

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Because of its potency, the drug is often effective in patients refractory to other uricosuric agents. Patients can usually be maintained indefinitely on it without cumulative effects or development of tolerance.

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*Kuzell, W. C., et al.: Effect of sulfinpyrazone on serum uric acid in gout: a long-term study, Geriatrics 19:894, 1964.

Photographic Contest

The Editors of Minnesota Medicine, in collaboration with the Doctors' Photographic Society of Minneapolis, take pleasure in announcing a monthly photographic contest. The contest is to promote an interest in photography in the medical profession. First prize each month will be publication in full color of the winning picture in Minnesota Medicine.

The following rules will govern the conduct of the contest:

1. Only doctors of medicine are eligible to submit pictures, and the picture must have been taken or composed by a physician.
2. Each contestant may submit not more than two pictures each month.
3. Only color transparencies, 35 mm. to 2¼", can be considered.
4. Each slide should be labeled with the maker's name, address, and the identifying title.
5. Slides should not be mounted on glass, but can be protected in plastic sleeves or envelopes.
6. Each entry must be accompanied by a self-addressed, stamped envelope if return of the picture is desired. Returns will be made shortly after the close of the contest each month. The winning photograph will be retained but will be returned after it has been used.
7. The deadline date for entry will be the 10th of each month and the winner of each month's contest will be announced in Minnesota Medicine in the subsequent issue. The date of publication will be three to six months in advance.
8. There will be no limitation on subject material except as indicated in item 10.
9. Model releases will be requested of winners where appropriate.
10. Judges will be selected by the editors of Minnesota Medicine and the Doctors' Photographic Society. The judges will be guided by the precepts of the Photographic Society of America, and winners will be based on appropriateness, interest, impact, and technical excellence.
11. The editors of Minnesota Medicine and the Doctors' Photographic Society cannot be responsible for entries lost or damaged, but every effort will be made to protect submitted pictures.

Your pictures are hereby invited. Please submit pictures to:

Photo Contest Editor
Minnesota Medicine

History of Medicine

Robert Koch

(1843-1910)

> *"Before microscopic forms can be regarded as the cause of contagion in man they must be found constantly in the contagious material, they must be isolated from it and their strength tested."*
> —*Jacob Henle*
> *Patholotical Researches, 1840*

Robert Koch initiated modern bacteriological technique, elevating bacteriology into the position of a separate science. To him we owe the main basis of the technique by which diseases are now studied.

Born into a large impoverished German family, it appeared certain that Koch would be obliged to learn the shoemaker's trade. However, the family's financial condition improved to the extent that he was able to go to Gottingen to study medicine, where he became a pupil of the great Henle. After graduation, he settled in the town of Rachwiz as a general practitioner. He served in the Franco-Prussian war, following which he resumed practice as district-physician of Wollstein.

His career in research began in 1872 when his wife gave him a birthday present of a microscope. This obscure physician, without university or research institute affiliation, worked not in a laboratory, but in his own home. Located in an agricultural region where anthrax was common among sheep and cattle, it was in the microscopical study of this disease in rabbits that Koch made his first great discovery. "He it was who first laid bare the natural history or life story, of the anthrax bacillus, and showed how to grow the bacillus, and how to obtain it unmixed with other organisms in 'pure culture' . . . Koch showed how to grow the organisms on solid media. He showed also that different organisms took up different dyes from a solution, so that they could be distinguished one from another by observing what color they took on when dyed with different chemicals."[1]

At the end of ten years of research Koch was the . . . "first to work out the complete life-history and sporulation of a bacterium. At that time bacteriology was a department of botany, and Ferdinand Cohn, the great botanist of Breslau, was the leading authority on microscopic plants. Whoever wanted information on the parasitism of Algae and Fungi, applied to Ferdinand Cohn. In the spring of 1876, Koch wrote to Cohn: 'After many vain attempts, I have finally been successful in discovering the process of development of the anthrax bacillus. After many experiments, I am able to state the results of these researches with sufficient certainty. Before, however, I bring this into the open, I respectfully appeal to you, esteemed Herr Professor, as the foremost authority on bacteria, to give me your judgment regarding this discovery.' "[2]

Cohn not only agreed to see Koch himself; he also invited some leading investigators of that day to witness the new methods. Among them was Professor Conheim, the foremost experimental pathologist of Europe. So down to Berlin came the unknown country doctor with his cultures of anthrax, a little doubtful himself as to whether or not he was on the right track. Professor Conheim was greatly impressed with Koch, hailing his

Continued

discovery as one of the most brilliant in the world. He had grasped the significance of it at once. Through his efforts Koch became a member of the Imperial Sanitary Commission in Berlin. In that way he could continue his research there. "Koch's accomplishments wrought a transformation in the health department . . . and in 1881 he dwarfed all his associates by his scheme of spreading liquid gelatin with meat infusion on glass plates, thus producing transparent solid media for pure cultures. This poured-plate method may be regarded as Koch's greatest single achievement, for there is no other method by which the bacteriologist can grow, isolate and recover pure cultures."[3]

(Continued next month.)

History of Medicine in Wright County*

Stephen J. (or J. S.) Wooster, occasionally spelled **Worcester,** came to Cokato in 1882 and practiced there through 1886. In August, 1882, when his arrival in Cokato was expected, the newspaper called him "Dr. Worcester from Wyzata." Dr. Wooster was a charter member of the Crow River Valley Medical Society (the forerunner of the Wright County Medical Society) when it was organized in 1883 and was a signer of its articles and by-laws. He was elected treasurer at the meeting in October, 1883.

In 1886 he is listed in Cokato as the only physician. He was a graduate of the College of Physicians and Surgeons, Keokuk, Iowa in 1882, was licensed in Minnesota October 1, 1883 and registered in Wright County on December 10 of that year. The "Official Register of Physicians, Minnesota, 1883-1890" state that he "removed from the state;" this must have happened not later than 1890. He must have returned to Minnesota as he is listed in Annandale in 1898 and 1900 and later was with his son in Rockford.

C. A. Wright, apparently started practice in Howard Lake in 1875. His card appeared first in the *Wright County Eagle* on February 3 of that year; he presents himself as an "homeopathic physician and surgeon; all calls promptly attended to." Medical directories list him there through 1893 (but no longer in 1896). Dr. Wright owned a 210 acre farm — on the Watertown Road on the Crow River, halfway between Delano and Watertown. He offered it for sale in February, 1884.** In April of that year he was elected surgeon of the Goodsell Post No. 86 G.A.R. at Howard Lake.† It seems he was a great hunter as the papers mention several times his trips to the prairies (1884 and 1885) and at one of these (November, 1885) he claimed to have killed five deer. In December, 1885 a news item mentions that he and a couple of other men were getting ready for an extended trip to California via Kansas.‡ Nothing more is known about him. There is no information of his background, where he came from or where he moved to.

(To be continued next month)

John J. Catlin, M.D.
Buffalo, Minnesota
Robert Rosenthal, M.D.
St. Paul, Minnesota

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*See Minnesota Med 48:965, 1965.
**Delano Eagle, February 28, 1884.
†Delano Eagle, April 17, 1884.
‡Delano Eagle, December 10, 1885.

Frugality. Make no expense but to do good to others or yourself; i.e., waste nothing.
— Benjamin Franklin

Physicians, Nurses Often Fail to Communicate, Says Professor of Nursing

The nurse and the physician work side by side in the hospital but frequently fail to understand one another.

The ultimate loser in any failure of doctor-nurse communication is the patient. If, for example, the nurse does not fully comprehend a doctor's orders regarding a patient, the patient suffers. If a doctor does not understand the nursing hierarchy in a hospital, he may issue orders which by their very nature are difficult for the nursing staff to carry out — and again the patient suffers.

"Nurse-Physician Communications in the Hospital" was the subject of a special program recently at the 114th annual convention of the American Medical Association. Sponsor of the session was the AMA Committee on Nursing.

"Communication difficulties appear to be related to the social structure of hospitals," said one of the speakers, Luther Christman, Ph.D., R.N., associate professor of nursing at the University of Michigan, Ann Arbor.

"For instance," he said, "vast educational differences exist between doctors and nurses. Training and education create vital differences in the way physicians and nurses see events in the hospital. In addition, the physician remains oriented to continued learning through postgraduate education, while the nurse's formal education usually stops the day she leaves training." In time, Dr. Christman added, the trend toward baccalaureate education and graduate training for nurses may reduce the educational gap.

As other critical areas of communication difficulty due to hospital social structure, he cited:

1. The various and often highly specialized technical languages of subgroups in the hospital. Nurses may lack the training to understand a highly technical order, but may be hesitant to ask for clarification. "People do not like to admit they do not understand, particularly if the communicator is a superior . . . thus the physician may leave the ward believing he has communicated only to be chagrined, and perhaps irked, when he finds this is not the case." Dr. Christman noted the best trained nurses are often placed in administrative positions where they contribute least to doctor-nurse understanding.
2. The differing career patterns of the two professions. Physicians are often self-employed and self-directing. Nurses are employees subject to control from the hospital medical staff, hospital administration, and nursing administration. If physicians assume that nurses have the same degree of self-direction as themselves, misunderstanding may result.
3. Socioeconomic class differences between members of the two professions. Physicians usually enjoy considerably larger incomes than nurses, permitting a different style of life that seldom brings them into social contact with members of the nursing staff. Also, physicians traditionally come from families with professional and business backgrounds while nurses most often come from working-class and lower-middle-class families; both groups take their social perspectives into training with them.
4. Sex differences, since most physicians are men and most nurses women. Normal cultural patterns of presumed male dominance and superiority are probably in effect during doctor-nurse professional contacts.
5. Clashes over power. The physician's accustomed position as a power unto himself in his office, and his intense preoccupation with the clinical problems of his patients in the hospital, may bring him into conflict with nurses when he is expected to share power in the complex organizational structure of the hospital.

"The hospital social structure can be made to help rather than hinder communication, if doctors and nurses cooperate in changing it," Dr. Christman said.

Among changes he recommended to facilitate physician-nurse understanding:

1. The employment of non-nursing personnel to perform non-professional administrative duties now being carried out by nurses, thus releasing many of the best educated nurses for patient care.
2. Improve the salaries of nurses. Physicians could help improve the climate between themselves and nurses if they actively supported moves for better nursing salaries.
3. Fostering of liaison committees between state medical societies and state nurses associations.

Continued

4. Organizing joint clinical workshops on state or district levels.
5. Sponsoring of joint research in improvement of patient care.

Also speaking on the program yesterday was Barbara Bates, M.D., Department of Medicine, University of Kentucky, Lexington.

Dr. Bates told of actual research done on the problem of nurse-physician communications by means of a questionnaire circulated to doctors and nurses in a university teaching hospital.

Each person receiving the questionnaire was asked to report specific incidents concerning the behavior of members of the other group, and how such incidents affected the patient.

Of the 839 replies received from nurses and the 475 from physicians, a total of 367 involved communication by either a doctor or nurse. Some incidents were examples of poor communication where the patient suffered, others were reported as illustrations of good doctor-nurse communication helping the patient.

Moderator of a reacting panel discussion was Edward G. Benz, R.N., director of nursing at Embreeville State Hospital, Embreeville, Pa.

Partnership Disability

We plan to publish an article on "Partnership Retirement." The theme of this article is that retirement provisions, beyond the value of the retired partner's assets and accounts receivable, are basically the financial responsibility of the individual partner, and not the collective responsibility of the partnership.

Restating our premise, that the primary goals of a partnership should be higher quality of practice and maximum ease of practice, there is little logic for a partnership assuming the economic responsibility for either retirement or disability of its members. On the contrary, the ill-advised assumption by a partnership of these financial responsibilities may prove to be a complete financial impossibility.

We have read proposals by various proponents of funding disability through a partnership. These proposals vary all the way from a few months of protection to lifetime indemnity. Some of the long-term proposals advocate funding by insurance after a certain period of time.

Simply analyzed, long-term disability protection funded out of earnings is economically impossible since it must come from reduced earnings of other partners. Disability insurance purchased through the partnership is impractical since there is no tax advantage and each partner ends up paying his own cost. The major disadvantage of an insured plan is that several partners may end up with insurance in amounts and types, and with companies that would not be their individual choice in a personal program. In our opinion, a disability provision which will provide a smooth transition for the disabled partner until *his* insurance program takes over, and one which gives realistic recognition to the financial equity of the disabled partner and the earnings of the remaining partners, is the only valid approach to partnership disability.

The most common disability arrangement in a partnership is one which provides guaranteed earnings continuation for the first three to twelve months of disability. For example, three months at 100%, three months at 75%, three months at 50% and three months at 25%. At the end of this period, the disabled partner's status must be appraised. If disability appears to be long-term or permanent, the disabled partner's interest will generally be terminated. If it appears he will return to work in a reasonable period, his earnings can be "suspended" until he returns.

Whatever the final specific provisions, partnership indemnity must represent realistic interim earnings, to be replaced by the disabled partner's individual insurance program for long-term protection.

An excellent principle to adhere to in discussing problems such as this in a partnership is to place yourself in the position of both the disabled and the remaining partner and consider all contingencies. If a proposal can survive this test and all partners agree to the logic of being the payor as well as the recipient, then the plan may have merit.

William D. Huntington*
Minneapolis, Minnesota

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*Northern Division Manager, Professional Management Midwest.

Doctors like fees no doubt — ought to like them; yet if they are brave and well-educated, the entire object of their lives is not fees. They, on the whole, desire to cure the sick; and, if they are good doctors, and the choice were fairly put to them, would rather cure their patient and lose their fee than kill him and get it.
— John Ruskin

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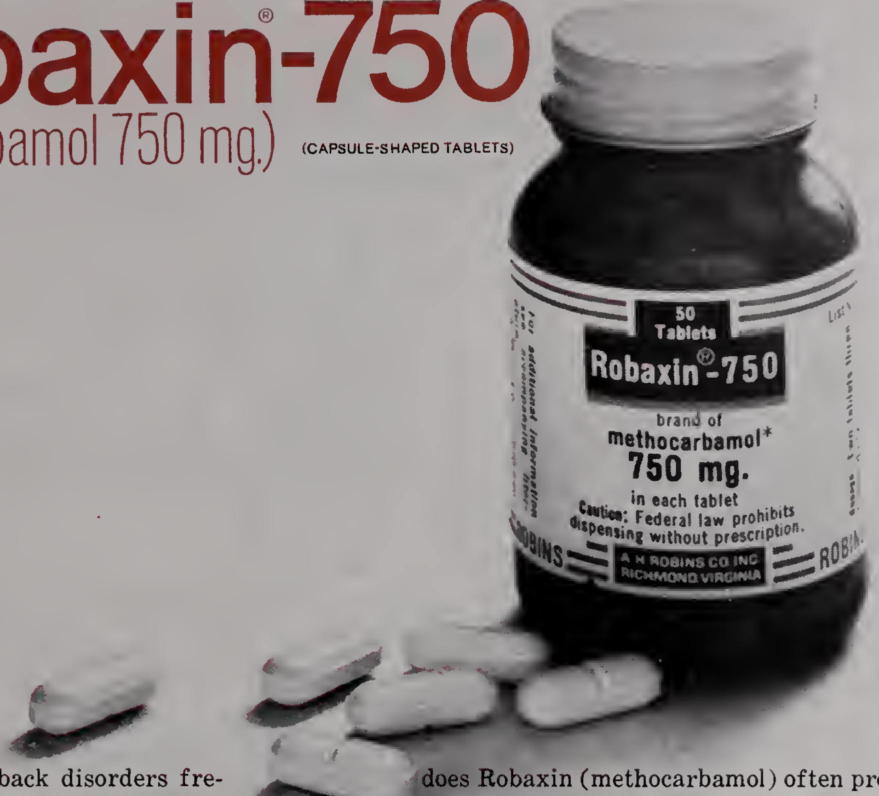

It has been noted that low-back disorders frequently "... are caused by truly mechanical conditions which yield to conservative treatment."[1] Basic to this conservative treatment are bed rest, a board for the bed, and applied heat. In addition, a good muscle relaxant is often helpful, as "... muscle relaxants are useful in chronic as well as acute low backaches."[4]

Robaxin (methocarbamol) has relieved spasm and pain in cases where the patient "had not responded to conservative measures prior to drug therapy."[6] A 100-patient study showed that Robaxin provided greater relief of muscle spasm for a longer period of time without adverse reactions "than any other commonly used relaxants...."[6]

A well-tolerated[7] skeletal muscle relaxant with "specificity of action,"[7] methocarbamol leaves normal muscle tone unaffected. Moreover, there is little likelihood of sedation[7]—a considerable advantage for the patient who must remain active and alert on his job.

Significantly, clinicians advise using a muscle relaxant "early and in adequate dosage."[8] In this regard, Robaxin (methocarbamol)—*particularly in the 750 mg. dosage (2 tabs. q.i.d.)*—offers optimal therapeutic benefits without a significantly increased incidence of side effects. And just as it works well as part of the basic regimen for low-back pain, so also does Robaxin (methocarbamol) often provide muscle relaxation in such conditions as musculoskeletal injury, chronic neurological disorders, and orthopedic situations.

BRIEF SUMMARY—Robaxin (methocarbamol) Tablets: Contraindicated in hypersensitive patients. Side effects (light-headedness, dizziness, drowsiness, nausea) may occur rarely, but usually disappear on reduced dosage. Hypersensitivity reactions develop infrequently.

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Miracle Mile Station, Minneapolis 16, Minn.

Winning Essay

The Advantages of Private Medical Care

James Kramer
Holy Trinity School
Rollingstone, Minnesota

This essay won second national prize of $500 in the 1965 Association of American Physicians & Surgeons Essay Contest.

When the proposed plan of medicare was first exposed to me, I realized that I knew very little about the problem or situation which the United States faces. I therefore made a study of all the facts concerned and came to the conclusion that private medical care has great advantages over the compulsory medicare plan. The reasons for my conclusion are summed up in this essay.

First, let us look at the magnitude and seriousness of the problem concerning our elderly persons.

Income of Elders Not Inadequate

The incomes of the aged, persons over 65, are inadequate for even a modest level of living. This has been said by advocates of federalized medicine. Let us look deeper into this and other statements which are deceptive in analyzing the economic and health conditions of the aged. For instance, the above statement was established by measuring the income of a mythical aged couple living in a hypothetical metropolitan city against the Labor Department's level of adequacy. However, the income figure used was not that of the elderly couples dwelling in metropolitan areas, but that of all elderly couples in the nation, including those in rural areas where the cost of living is substantially less. Excluded from this fictionalized situation are the U. S. Department of Labor figures which show that the income of the aged dwelling in metropolitan areas is significantly higher than the national median.

Fewer Obligations

Elderly couples have fewer family obligations, less debt, more homes mortgage free, and they enjoy special tax advantages. Between 1960 and 1961 the income of families headed by an older person rose more than twice as much as the increase of all families. A University of Michigan survey showed that 96% of all the aged did not owe any money to a doctor, dentist, or hospital. Also stated was the fact that of medicare expenditures of persons over 65 in 1961, 3.8 billion or nearly three-fourths of the total expenditures were paid from private sources.

Elders Not Universally Frail

Proponents of federalized medicine repeatedly portray our aged as universally frail, feeble and constantly ill. This is achieved by declaring that the elderly visit doctors 36% more than younger people, and that four-fifths of our aged has one or more chronic illness. These statistics are misleading because: the 36% visits can be translated to only 1.8 more visits per year, and "chronic illness includes non-disabling afflictions such as hay fever and varicose veins." Thus 84.5% of the aged either has no chronic condition or is without serious limitations of major activity.

In this summary of statistics I am trying to convey the opinion which I concluded,

Continued

that is, many of the aged can afford the health care they need without federal aid.

Undoubtedly there are many people who are not inclined to share my opinion on the economic and health conditions of the aged. The results are bills introduced providing medical care for the aged of which the most recent is the King-Anderson Bill. At this time a discussion of this bill is appropriate.

Many Not Covered

The proposed bill would provide limited health care benefits for everyone over 65 under the Social Security and Railroad Retirement Acts, and some 2,500,000 persons who are 65 and over not covered by the two acts. It would provide 45 days of hospital care free, or 90 to 180 days of nursing home service under certain conditions, diagnostic services above the first $20, and some other health services.

Drugs and Doctors Fee Not Covered

Now let's look at the other side of the picture, by pointing out some health care benefits which are not provided by the bill. It would pay practically no doctor bills. Any drugs or devices outside a hospital would not be furnished, as well as the cost of diagnosis as not part of a hospital service. It would provide no help for those confined in mental or tubercular hospitals. In other words, "it would cover less than one-quarter of the total yearly health care costs of the average aged person."

Cost Underestimated

Additional grounds of disapproval to the bill are its cost and its provision of a "free choice" in seeking health care. For the bill's first year in operation, the cost has been estimated at from $1.4 billion to $25 billion and England's socialized medicine program now costs nearly five times the original estimates. Also, the bill claims to give a free choice in medical care services, yet only participating hospitals, physicians on the staff of participating hospitals, and nursing homes affiliated with such a hospital are eligible to the program. Thus, personal physicians and preferred nursing homes might be disqualified. From these facts, I find not only the proposed bill unfavorable and inadequate for the health care of our aged, but also find its implications dangerous.

Questions may now arise in your mind, as they did in mine, concerning what provisions there are for health care of the aged in our contemporary society.

Health Insurance Available

First, can the aged get health insurance? The answer is yes. Today 450 insurance organizations now offer hundreds of policies available to all aged. They offer a wide range of choice in benefits and premium costs. More than 60% of the aged are now protected against the cost of illness through health insurance.

Second, are there any provisions today for the aged that need financial help? Yes, the Kerr-Mills Law was passed by Congress in 1960. This bill has two objectives, one, to improve and establish state health care programs for the needy, and two, establish new health care programs for the near-needy. Through this program, the federal and individual state governments work together to guarantee every aged American the health care he needs. The Kerr-Mills Law has many advantages over the proposed Medicare Bill. It permits individual states to develop and change their programs as experience shows changes to be desirable. Free choice of hospitals and doctors is mandatory under state programs. This program helps only those who need help, thus avoiding waste of tax dollars.

Reports prove that the Kerr-Mills program has been a successful program. "Thousands of needy and near-needy older persons across the nation are receiving medical, hospital and nursing home care every day under Kerr-Mills program." Furthermore, over 93% of 17.5 million aged live in states which adopted the Kerr-Mills program. The few states not adopting this program feel that existing state and local programs are taking care of their needs.

The conclusion I have drawn is that there are adequate provisions for the health care of the aged under private insurance organizations and existing programmed financial aid.

Principle of Subsidiarity

I feel an important question in the controversy over Medicare is, whether federalized medical care complies with the ideals set forth in the Principle of Subsidiarity. The Principle of Subsidiarity, as I have interpreted it, is the standard for deciding which functions the government should assume and which it should leave to individuals and lesser groups. This principle steers a course between two extremes, Individualism, through which the government is limited to the negative function of maintaining order, and Collectivism, through which all social functions are given over to the state. According to the Principle of Subsidiarity, it is wrong to hand over to the government that which individuals or individual groups can accomplish through initiative and enterprise. In the arguments which I have brought forth, I have tried to show that individual groups can accomplish the duty of providing health care for the aged. Therefore, I find it dangerous to transfer this duty to the Federal government.

Professional Freedom Endangered

From the point of view of the medical profession, professional freedom is an important part of the American way of life. This freedom has given the American Medical Profession the high position of respect that it holds in the world today. Its contribution to medical science has caused the countries of the world to look to America for the alleviation of their medical problems. Although the Medicare Bill won't provide complete absence of professional freedom, many fear that this bill will lead to that. Federalized medicine, I feel, would endanger the quality of our medical care. I do not stand alone in this evaluation in that the American Medical Association and doctors openly convey the same opinion in quotes such as, "I sincerely believe that the free practice of medicine, which has given our people the best medical care in the world, is in jeopardy."

Loss of Individuality

Three conditions are brought about when the government finances and operates medical services to some extent. *First,* the relationship between the patient and the doctor is not wholly voluntary. Therefore, the patient won't have full confidence in the doctor and the doctor won't have his heart fully in his work. *Second,* when the doctor is paid by the Government and not by the patient, he comes to work for the Government and not the patient, thus degrading the quality of medicine. *Third,* incentive is lost, and it is essential for good medical practice that there be maximum incentives for the doctor to do his best work and constantly improve himself.

Inadequate Supply of Student Doctors

Greater federal activity in health care would cause many medical students to abandon their study and others to leave the United States upon graduation. It's a known fact that we have a shortage of good doctors in our country today, therefore, not only the quality, but also the quantity of health care could decrease. Professional freedom is essential for an adequate supply of physicians and a high quality of medicine.

Conclusion

Through these facts and arguments which I have presented I have attempted to support the stand I hold on the Medicare issue. From this research I draw the conclusion that private medical care is highly advantageous for the following: the taxpayer . . . costs of taxes won't soar; the aged . . . free choice in medical care; doctors . . . freedom of profession and quality medicine; our governmental system . . . private enterprise will remain to thrive; and my future . . . a free society surviving and flourishing.

Test Every Patient for Diabetes
Diabetes Week, November 14-20

Paleopathology III: Egypt*

What diseases ancient Egyptians endured are partially recorded in mummies which underwent roentgenographic examination by Roy Moodie in his capacity as Paleopathologist for the Wellcome Historical Museum in London, the results of which were published in the Anthropology Memoirs of the Field Museum of Natural History, which in 1926 established a Division of Roentgenology to study ancient morbidities and disabilities.

In examining the mummies at the Field Museum special care had to be exerted to distinguish between actual body bone and tissue on the one hand, and extraneous materials on the other: sand and other detritus intruded by time and nature, as well as burial artifacts inserted by survivors. Furthermore, the mummy remains were sometimes so altered by embalming substances and so mutilated by vandals as to obscure and distort the pictures from which the data were to be derived.

Found to be prevalent, however, were numerous familiar pathologies such as arthridites, fractures with and without callus, and arteriosclerosis — occurring, curiously, among both young and old alike, and due to no known dietary cause. Also in Egyptian mummies paleopathologists have found evidences of pneumonia, smallpox, necroses, tumors, alveolar osteitis, and cirrhosis of the liver.

That these early people suffered from renal disease is apparent from traces of abscesses and of calcified bilharzia eggs in their kidneys. Schistosomiasis was not uncommon. Hypertrophied spleens demonstrate damage from malaria. A case of hydrocephalus was observed — with partial paralysis on one side. The mummy of one young adult presented evidence of a psoas abscess associated with either Pott's disease or tuberculosis. In the catacombs at Alexandria another mummy revealed a pelvic osteosarcoma.

Apparently spondylitis deformans was not rare among ancient Egyptians; Nefermaat of the Third Dynasty (2980-2900 B.C.) exhibited a solid bone block from the fourth cervical vertebra to the coccyx. Some mummies show Bouchard's nodosities, an indication of gastrectasis. Osteoporosis of the skull resulting in patches of porous bone was also common — due doubtless to some unidentified nutritional disturbance.

Paleopathologist Marc Ruffer made a special study of the mouth and teeth in ancient Egyptian mummies and found impaction, attrition, caries, abscesses and fistulae, periodontitis, and particularly absorptive osteitis due to pyorrhea: that ubiquitous and perennial scourge present on the evolutionary ladder from fossil animal right up to modern man.

Specific search was made by Mr. Moodie for evidence of calculi in the Egyptian mummies under scrutiny, but none was found in the kidneys, gallbladders, or urinary bladders of the individuals he examined and reported on. Roentgen rays, however, fail to reveal all of the lesions possibly present in wrapped mummies, such as trepannings, club injuries, slingshot wounds, and linear fractures, these being apparent only on more direct examination of the remains.

On the basis of 15 Egyptian mummies studied the incidence of disease was estimated at 40 per cent. However, a study based on larger numbers might well show a lower incidence. Nevertheless, the figures available are significant and challenging in the long-range perspective on man and his diseases.

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*See Minnesota Med 48:908 and 48:1020, 1965.

Meetings and Announcements

A work of real merit finds favor at last. — A. B. Alcott

SEPTEMBER

Zumbro Valley Medical Society, September 1, Plummer Hall, Mayo Clinic, Rochester.

St. Louis Co. Medical Society, Executive Comm., September 9, 6:00 p.m., St. Mary's Hospital, Duluth and Regular Meeting, 8:00 p.m.

Minnesota Heart Association, Annual Meeting, Scientific Sessions, September 18, 9:00 a.m. — 5:00 p.m. (Place unknown).

Minnesota Medical Foundation, Annual Meeting, September 27, 8:00 p.m., Mayo Auditorium, University of Minnesota, Minneapolis.

Minn. Academy of General Practice, House of Delegates, 4:00 p.m., September 28, Hotel Radisson, Minneapolis.

Minn. Academy of General Practice, Fall Refresher, Radisson Hotel, September 29-30, Minneapolis.

Ramsey Co. Medical Society, Business Meeting, 8:00 p.m., 15th Floor Lowry Medical Arts Bldg., St. Paul, "Nominations for Officers," September 27.

Annual West North-Central Interprofessional Seminar on Diseases Common to Animals and Men, University Hospital in Iowa City, Iowa, on September 16-17. Contact: Dr. W. F. McCulloch, Institute of Agricultural Medicine, University of Iowa, Iowa City.

Southern Minnesota Medical Association Meeting at the Sheraton-Ritz Hotel in Minneapolis, September 10th. Contact: John Eustermann, M.D., Mankato Clinic, Mankato, Minnesota.

Department of Otolaryngology, College of Medicine of the University of Illinois at the Medical Center, Chicago, will conduct a postgraduate course in laryngology and bronchoesophagology September 20-October 2. Write: University of Illinois Medical Center, Post Office Box 6998, Chicago 60680.

Seventh Annual Methodist Hospital Symposium — Methodist Hospital in Minneapolis. September 11th.

Fall Meeting of Minnesota Radiological Society, Ruttger's Lodge, Brainerd, September 11. Carman Lecturer will be Dr. Harold Jacobson of Montefiore Hospital, New York City. Contact: E. A Peterson, M.D., 572 Lowry Medical Arts, St. Paul.

Northwestern Pediatric Society Fall Meeting, September 24, White Pine Inn, Bayport, Minn. Contact: W. D. Bevis, M.D., 301 Kenwood Parkway, Minneapolis.

45th Annual Meeting of the Northern Minnesota Medical Association, Crookston, September 10-11th. Post graduate refresher program geared to diabetes and related subjects. Program will begin at 8:30 a.m. with registration at Elks Club. Contact: R. H. Puumala, M.D. Cloquet.

OCTOBER

American Fracture Association Meeting, Las Vegas, Nevada on October 24-28. Contact: W. Compere Basom, M.D., 1220 N. Stanton St., El Paso, Texas 79902.

Annual Meeting of the Academy of Psychosomatic Medicine, October 11-13, Sherman House, Chicago. Edwin Dunlop, M.D., 150 Emory St., Attleboro, Mass. 02703.

51st Annual Clinical Congress of the American College of Surgeons, October 18-22, Atlantic City, New Jersey, Dennis and Shelburne Hotel. Contact: College.

Third Fall Meeting of the American College of Physicians, October 7-9, Deauville Hotel, Miami Beach, Florida. Contact: Edward Rosenow, Jr., M.D., 4200 Pine Street, Philadelphia, Pa.

Annual Otolaryngologic Assembly of 1965 will be held October 30 through November 5, in the new Illinois Eye and Ear Infirmary at the Medical Center, Chicago. Contact: University of Illinois, P.O. Box 6998, Chicago.

Annual Course in Postgraduate Gastroenterology of the American College of Gastroenterology, Americana Hotel in Bal Harbour, Florida, October 28, 29, 30. Contact: College, 33 West 60th Street, New York, N. Y. 10023

American College of Nutrition Annual Scientific Meeting, Americana Hotel in New York City, October 10th. Contact: R. A. Peterman, M.D., 3 Craig Court, Totowa Borough, New Jersey 07512.

American Academy of Pediatrics 34th Annual Meeting, October 23-28, Palmer House, Chicago. Write: Academy, 1801 Hinman Avenue, Evanston, Illinois.

American Association of Automative Medicine Meeting, October 22-23, Mayo Clinic, Rochester. Write: Postgraduate Courses, Mayo Clinic, Rochester, Minnesota 55902.

Continued

MEETINGS AND ANNOUNCEMENTS

NOVEMBER

Inaugural Scientific Program of the new Ancker Hospital, St. Paul, will be held November 11-13. Program will include two days of general medical meetings. Contact: James F. Hammarsten, M.D., Ancker Hospital, St. Paul.

Wisconsin Society of Pathologists Meeting, November 13-15, Pathology Department, Marquette University, School of Medicine, Milwaukee. Contact: Joseph L. Teresi, M.D. at 561 North 15th St., Milwaukee.

ANNOUNCEMENTS

Hahnemann Medical College & Hospital, Philadelphia, postgraduate courses:

Nov. 22-24 — Symposium Cancer Chemotherapy, Sheraton Hotel.

* * *

A nine month tutorial program in Cardiology, September 15, 1965 to June 15, 1966, will be offered by Institute for Cardio-Pulmonary Diseases, Scripps Clinic and Research Foundation, La Jolla, California. For details: Write E. Grey Diamond, M.D., Scripps Clinic and Research Foundation, La Jolla, California.

* * *

The University of Minnesota Department of Pediatrics continuation course in pediatrics, September 21-23, University of Minnesota Campus in Minneapolis. "Genesis, Epigenesis, Modern Physic and the Child" is the subject. Contact: Edward Defoe, M.D., Department of Pediatrics, University of Minnesota Hospitals, Minneapolis 55455.

* * *

Three day meeting in Cardiology at the Lowry Hotel, St. Paul, September 15-17, under the sponsorship of the Council on Clinical Cardiology of the American Heart Association, the St. Paul Medical Center, and the Minnesota Heart Association.

The focus of this three-day postgraduate course will be on functional pathology of valvular and pericardial diseases — congenital and acquired types.

The course will be directed by Jesse E. Edwards, M.D., Director of Laboratories at Charles T. Miller Hospital and board member of the American Heart Association. Doctors Lewis S. Carey, Robert S. Eliot, James N. Karnegis and James Ronan will be on the faculty.

Happiness is that peculiar sensation you acquire when you are too busy to be miserable.

— Mutual Moments

People are usually willing to meet each other half way, but their judgments of distances vary considerably. — The Rodney (Ont.) Mercury

Indications: Many types of edema involving retention of salt and water.
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Precautions: Reduce dosage of concomitant antihypertensive agents by at least one-half. Discontinue if the BUN rises or liver dysfunction is aggravated. Electrolyte imbalance and potassium depletion may occur; take special care in cirrhosis or severe ischemic heart disease, and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended.
Side Effects: Agranulocytosis, constipation, dizziness, dysuria, headache, hyperglycemia, hyperuricemia, impotence, leukopenia, muscle cramps, nausea, postural hypotension, purpura, thrombocytopenia, transient myopia, urticaria, vomiting and weakness.
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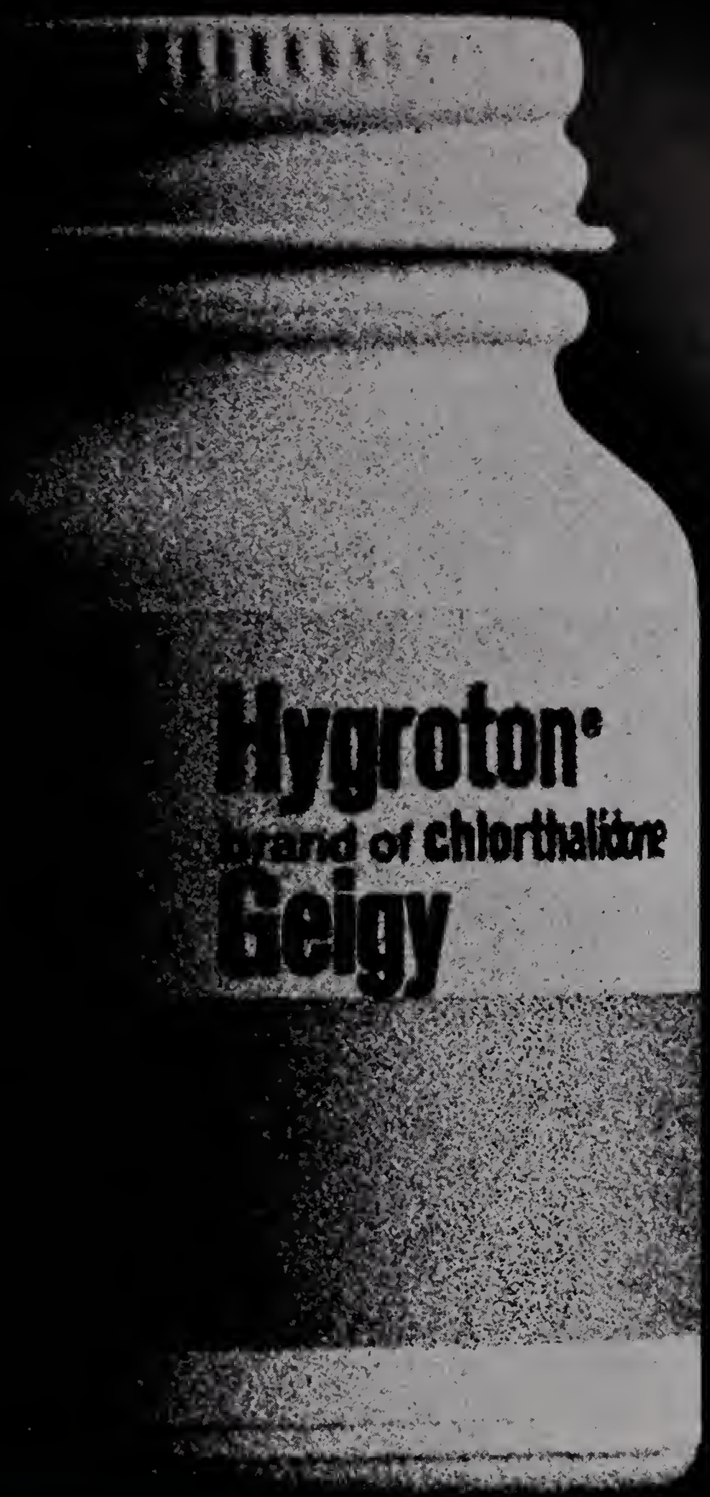

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Replies to advertisements with key numbers should be mailed in care of MINNESOTA MEDICINE, *496 Lowry Medical Arts Bldg., St. Paul, Minn. 55102*

WANTED PEDIATRICIANS AND INTERNISTS. Office space now available in new, modern, well established center — excellent opportunity for good earnings and professional pursuits — fastest growing suburban area. Write or phone A. G. Erickson, 7033 Edgewood Avenue North, Minneapolis Tel 533-7332.

WANTED: Board Certified or eligible internist to associate with group in large, active practice in Minneapolis. Group consists of Surgeon, Obstetrician, Pediatrician and Internist maintaining downtown and suburban offices. Partnership in mind. Contact: Jesse J. Barron, M.D., 1127 Medical Arts Building, Minneapolis, Minnesota 55402, FEderal 2-8259."

FOR RENT: Successful medical building. Opportunity for doctor to start new group. Rent at less than $3.00 square foot. Deluxe, modern, air-conditioned, all brick building with capacity up to four doctors. Located at 36th Avenue North and Noble Avenue in Northwest Suburban Minneapolis. For further information: Call Noble Drug at 588-9449 and ask for Ben or Lou.

MORGAN, MINNESOTA, Wants General Practitioner — present physician retiring after 33 years. Opportunity to take over well established practice. Progressive community in the best rural area of Southern Minnesota. Office space and equipment available. Call or write John Hageman, Pharmacist, Morgan, Minnesota. Telephone Morgan No. 96.

WHITE BEAR LAKE, MINNESOTA. A suburban community of 35,000 and growing fast. Available several ground floor air-conditioned suites in fireproof building in central business district, free municipal parking lot at second entrance in rear. See: N. R. Dittberner, 316 Washington Avenue, White Bear Lake. Telephone: Collect anytime 429-7787.

BUSY, GROWING aggressive 3-man partnership in Northwest Wisconsin serving a trade area of 15,000 needs a well-trained recent graduate with fulfilled military obligations to associate immediately on excellent salary, with partnership in 1 year if mutually agreeable. Modern 15 room air conditioned brick clinic building is being doubled in size this year. 32 bed hospital and new 42 bed nursing home one minute from clinic. New 1500 student consolidated school. Excellent hunting, fishing and outdoor sport facilities in immediate area. Contact: MINNESOTA MEDICINE — 317; 496 Lowry Medical Arts Building, St. Paul 55102.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE — 289; 496 Lowry Medical Arts Building; St. Paul, 55102.

WANTED: Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty seven bed hospital, X ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact: A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

PROFESSIONAL AIR AMBULANCE. Multi or single engine aircraft. All weather and night flight capability, anywhere in the U. S. Oxygen, Respirator, Aspirator, Nursing service, all medications. Also full time M.D. Board Anesthesiologist providing all medical care in flight available on request. MIDWEST AIR TRANSPORTS, Operations Office, Municipal Airport, Waterloo, Iowa, Phone 319-2331083.

A 13 MEMBER specialty group in the Midwest will need several men to replace and add to present staff. This has been a rewarding group for years, is now, and will be for years to come. We need 3 internists, 1 dermatologist, 1 ob-gyn, 1 pediatrician, 1 general and thoracic surgeon, 1 orthopedist, 1 ophthalmologist, 1 otorhinolaryngologist, and 1 psychiatrist. This is a very good town for a family man. Three colleges (1 a State College). Good schools and excellent recreation programs. Good hunting, fishing and water sports. Applicants should be Board certified or completing requirements. Write MINNESOTA MEDICINE — 324; 406 Lowry Medical Arts Building, St. Paul 55102.

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WANTED GENERAL PRACTITIONER OR SURGEON space available July 15th for party interested in a very active solo professional pursuit. Ideal air conditioned suite, an opportunity that must be seen. Contact A. G. Erickson, 7033 Edgewood Avenue North, Minneapolis, or phone 533-7332.

PART TIME INTERNIST OR GENERAL PRACTITIONER. Good compensation — Midway Area. Alfred F. Anderegg, M.D.; 2500 Como Avenue, St. Paul, Minnesota.

OPENING AVAILABLE — approved. First year surgical residency for physician planning on entering Residency Program in Surgical Specialties. For complete details write: Director of Medical Education, Saint Joseph's Hospital, 69 West Exchange Street, St. Paul, Minnesota 55102.

PSYCHIATRIC RESIDENCIES: Positions available July 1966. Fully approved; balanced didactic and clinical experiences. Five-year career program: $8,895, $10,294, $12,048, $15,368, $16,203; NIMH General Practitioner Stipends $12,000 annually for three years. In Michigan's Water-Winter Wonderland. Contact: Dr. M. Duane Sommerness, Medical Superintendent, Traverse City State Hospital, Traverse City, Michigan. An equal opportunity employer.

WANTED INTERNIST, Board qualified or certified for 22-physician mixed group of general practitioners and specialists (East Range Clinic, Virginia, Minnesota). Salary first year, then full partnership. Centrally located in area of rapidly expanding economy.

WANTED: one or two general practitioners. Excellent clinic and hospital facilities. Rural practice established 18 years. Salary open, partnership if compatible. Lloyd H. Klefstad, M.D., Greenbush, Minnesota.

GENERAL PRACTITIONER: well established multi-group specialty fourteen man group (seven GP's) Mid-western city, population 30,000; beginning salary then partnership; no investment; clinic building six years old; excellent school, hospital and recreational facilities. Write: MINNESOTA MEDICINE — 307, 496 Lowry Medical Arts Building, St. Paul 55102.

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SACRED HEART, MINNESOTA, doctorless since 1961, wants general practitioner. Population 700, accredited hospital 10 miles away. Write: Rev. Robert Bardy, Phone 765-2547, Sacred Heart, Minnesota.

INTERNIST: seven-man group desires services of another Board eligible internist. Located Central Minnesota. Approved 125 bed hospital. Excellent public and parochial schools. Junior state college. Close to State University and many private colleges. Marvelous fishing, hunting and golf facilities. Supervised youth activities. Salary negotiable. Full partnership available in eighteen months. Many fringe benefits. Write: MINNESOTA MEDICINE — 321; 496 Lowry Medical Arts Building, St. Paul 55102.

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On Bloodletting

A medical manuscript of the twelfth century expounds on the virtues of bloodletting:

It contains the beginning of health, it makes the mind sincere, it aids the memory, it purges the brain, it reforms the bladder, it warms the marrow, it opens the hearing, it checks tears, it removes nausea, it benefits the stomach, it invites digestion, it evokes the voice, it builds up the sense, it moves the bowels, it enriches sleep, it removes anxiety, it nourishes good health . . .*

The author is anonymous.

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*Thorndike, Lynn: A History of Magic and Experimental Science, Vol. 1, p. 728. The MacMillan Company, New York, 1923.

GERIATRIC SYNDROME

when a change in environment overwhelms him with anxiety

Failing health, financial difficulties, or the death of a spouse are among the reasons why elderly people may be obliged to leave their familiar surroundings. Moving in with children or entering a home for the aged may satisfy practical requirements but can be psychologically traumatic since emotional resilience tends to diminish with age.

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2. Gustafson, Jr. et al. Use of Glycine in the Treatment of Peripheral Vascular Disease, Surgery 25:539 (1949).

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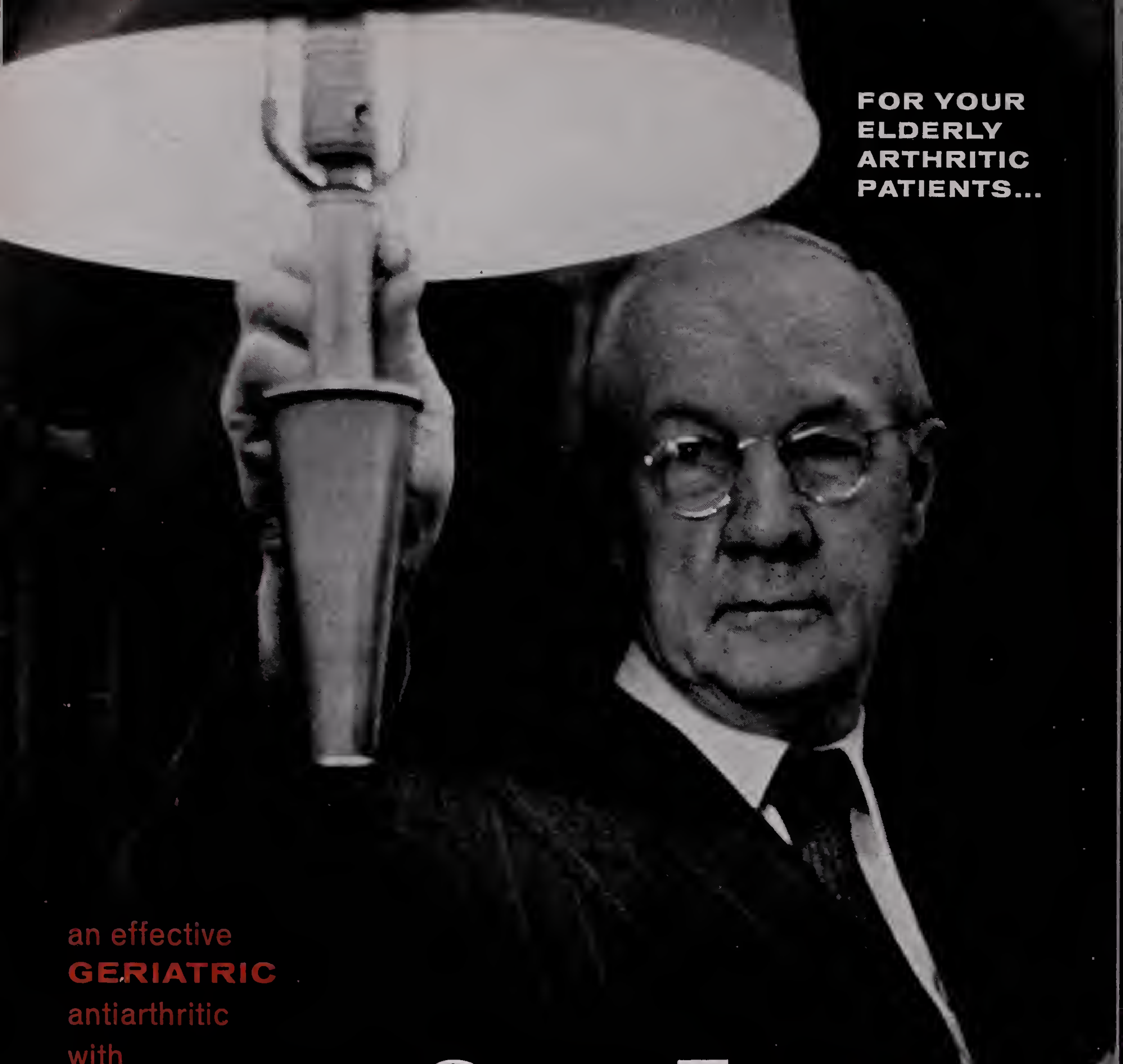

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Physician's Diary

Good company and good discourse are the very sinews of virtue. — Isaak Walton

The 75th Anniversary seal of the College of Medical Sciences, University of Minnesota, depicts the tree of life, one of the earliest medical symbols in ancient Eastern cultures. The pine cone, fruit of the tree of life, was believed to have both healing and supernatural powers.

* * *

Dr. Everett J. Schmitz was elected chief of the St. Cloud Hospital medical staff at the annual meeting of the group. Other officers elected were: **Dr. E. M. LaFond**, vice-chief of staff and **Dr. A. T. Rozycki**, secretary.

* * *

Dr. Randall G. Sprague, senior consultant in medicine in the Mayo Clinic, Rochester, was given the Banting Memorial Award of the American Diabetes Association for his original clinical investigations in metabolic diseases.

* * *

Dr. George C. Flora, assistant professor, psychiatry-neurology, and **Jack W. Miller**, associate professor, pharmacology, were the winners of the 1965 Minnesota State Medical Association's Distinguished Teaching Awards. Presentation was made by **Dr. J. Minott Stickney** of Rochester, President of the Association, during the annual medical awards day program at the University of Minnesota. The 1965 senior medical class graduates in the 75th anniversary year celebration of the establishment of the University of Minnesota Medical School with 148 members, the largest ever to graduate.

* * *

Dr. Laurentius O. Underdahl, head of a section of medicine in the Mayo Clinic, was elected president of the American Diabetes Association at its annual meeting in New York City, and **Dr. C. Allen Good**, head of the section of diagnostic roentgenology of the Mayo Clinic, was elected president of the American Board of Radiology, Inc. at its meeting of the board at San Francisco.

* * *

After twenty-nine years as obstetrician and gynecologist with the Worthington Clinic, **Dr. F. L. Schade**, has retired. It is believed that Dr. Schade has delivered more than 5,000 babies in Worthington. **Dr. and Mrs. Schade** plan to leave Worthington for ranch life near Santa Cruz, California.

Dr. William C. Bernstein, clinical professor of surgery at the University of Minnesota, was elected vice-president of the American Proctologic Society at its annual meeting.

* * *

NEW LOCATIONS: **Dr. Charles W. Quimby, Jr.** has joined the medical staff of the Community Memorial Hospital in Winona . . . **Dr. Roy Daumann** of Madison will join the Jackson Medical Center . . . **Dr. Robert Mathisen** of Fridley will practice in Annandale . . . **Dr. Darrel W. Siebert** opened up an office in Pipestone . . . **Dr. Arnold Overland** will leave the Klefstad Clinic in Greenbush to practice in Rolla, North Dakota . . . **Dr. James Schuft** is to leave Morris to specialize in radiology at the Charles T. Miller Hospital in St. Paul . . . **Dr. Arnold M. Berg** will leave Roseau to become an associate with the Falls Starekow Clinic in Thief River Falls . . . **Dr. Andrew N. Stiner** will begin practicing medicine in the Thielen Clinic in St. Michael . . . **Doctors Robert Conley, B. R. Geurs** and **A. M. Scheidel** have moved into new quarters in Mankato . . . **Dr. Bennie Faul** and **Dr. Bruce W. Wells** have joined the Worthington Clinic.

* * *

Dr. James R. Pluth, a fellow in surgery at the Mayo Clinic, received a surgical travel award for high achievement in surgery from the Mayo Graduate School.

* * *

Dr. E. A. Olson of Pine Island was recently honored for forty-one years of community service by that town. There was a parade, and a bronze plaque was presented to **Dr. Olson.**

* * *

Dr. James Nixon, Deerwood, has been appointed to serve as Crow Wing county coroner. Dr. Nixon, who is affiliated with the Cuyuna Range Clinic, will succeed **Dr. Maurice Meller.**

* * *

Dr. William H. Remine of the Mayo Clinic, was elected to president of the Minnesota Surgical Society at its meeting this month. **Dr. Harry Neel** of Albert Lea was named president-elect. **Dr. Jacob Strickler** of Minneapolis was chosen vice president and **Dr. Martin Adson** of Rochester was re-elected secretary-treasurer.

Minnesota Medicine at a Glance

Giant Russell Bodies, Schleicher Page 1125

Giant Russell bodies in neoplastic lymphoid cells have been reported but not extensively observed. This manuscript, with illustrations on the cover, is a masterful study and an excellent illustration of the giant Russell bodies in color.

A Cause of Gastrointestinal Hemorrhage, Myhre Page 1131

Though the usual cause of intestinal hemorrhage becomes readily evident, thrombocythemia has not been included in the list of causes for this gastrointestinal complication. It is well to keep in mind thrombocythemia as one of the possible causes of obscure hemorrhage, as detailed in this case report, and in a review of the literature.

Mediastinoscopy, Duvall & Koop Page 1135

Though there may be other methods of visualizing the mediastinum for masses, mediastinoscopy adds another method to the armamentarium of the surgeon who is desirous of making a full evaluation of the pathologic findings before making extensive surgical explorations.

Radioactive Isotope Scintiscanning, Loken Page 1138

Scintiscanning with the various types of isotopes opens a new field of exploration for visualization of many of the organs of the body. Visualization with a Geiger counter and the scanning produced is beautifully illustrated.

Tracheoesophageal Fistula, Calin and Mork Page 1144

The more common tracheoesophageal fistula seen in infants offers no problem, but the H-type fistula without atresia may be difficult to identify roentgenologically. When the clinical symptoms suggest, nevertheless, that a tracheoesophageal fistula does exist, cinefluorography with an exposure of 30 frames per second can be very valuable in establishing a diagnosis, thereby aiding the surgeon to do a definitive procedure which might otherwise be overlooked.

Neuropsychiatrist in a Court of Justice, Jeub Page 1147

This manuscript and the editorial on page 1155 are worth reviewing from the viewpoint of the neuropsychiatrist and that of the judiciary.

Dermatomyositis, Grand Rounds Page 1191

Dermatomyositis, a disease with a very grave prognosis, fortunately is not frequently seen, but when it is observed the outlook is universally fatal.

It begins insidiously with a variety of cutaneous manifestations, low grade fever, malaise, and minimal aches and pains in the extremities. In patients with atypical rheumatoid symptoms the disease should be suspected. The determination of an increase in the transaminase provides a valuable clue as to the continued progression of muscular necrosis which is evident in this disease. The use of steroids to suppress the inflammatory reaction of the muscle has been found to be of some clinical value, though the eventual prognosis continues to remain grave.

Antidepressant Drugs, Janecek Page 1197

Drugs for depressive symptoms are used in a variety of syndromes. There may be the grief-reaction syndrome, the endogenous syndrome in which the individual has a dismal, hopeless outlook and is severely impaired in self esteem; the repressed-rage syndrome; the pseudoneurotic schizophrenic syndrome, and lastly the maladjusted personality pattern.

The choice of drugs for these various syndromes is of significance, and it would be well to review this manuscript in order to have in mind general precautions to be observed in prescribing these drugs, as they may be inadvertently given to patients for whom they are not indicated.

Surgical Horizon, Wangensteen Page 1219

For a literary sketch of a surgical lifetime and a philosophy that has been engendered, the reading of this manuscript is well worth the half hour of pleasant reminiscences, into the history of medicine, which will be required to digest it.

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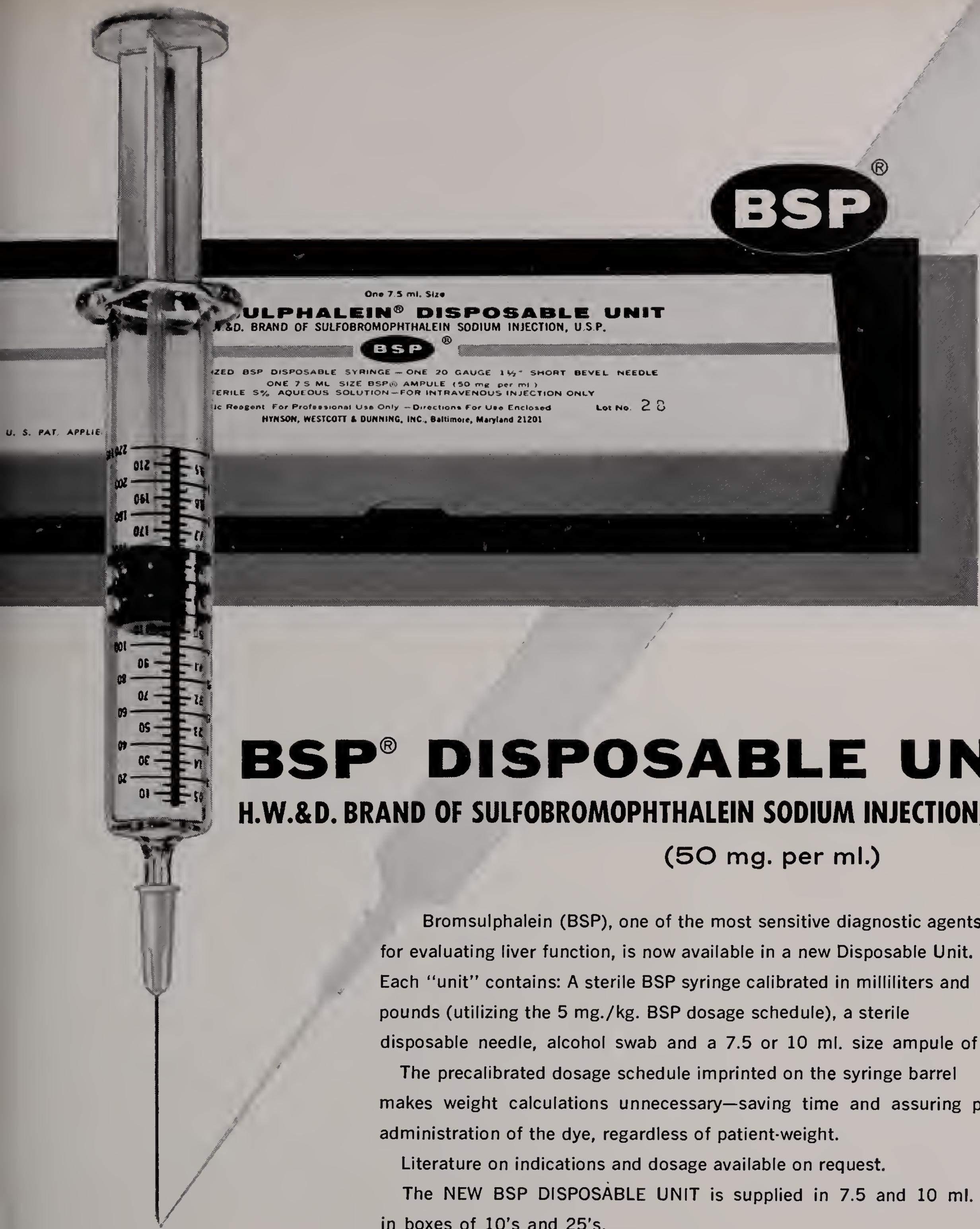
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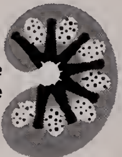

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Side Effects: The only side effect reported with a
frequency is sleepiness, usually on higher th
recommended doses. An occasional patient m
not tolerate carisoprodol because of an individ
reaction, such as a sensation of weakness. Oth
rarely observed reactions have included dizzine
ataxia, tremor, agitation, irritability, headache,
crease in eosinophil count, flushing of face, a
gastrointestinal symptoms.

One instance each of pancytopenia and leu
penia, occurring when carisoprodol was adm
istered with other drugs, has been reported, as
an instance of fixed drug eruption with carisopro
and subsequent cross reaction to meprobama
Rare allergic reactions, usually mild, have includ
one case each of anaphylactoid reaction with m
shock and angioneurotic edema with respirat
difficulty, both reversed with appropriate thera
In cases of allergic or hypersensitivity reactio
carisoprodol should be discontinued and approp
ate therapy initiated. Suicidal attempts may p
duce coma and/or mild shock and respirat
depression.

Dosage: Usual adult dose is one 350 mg. tab
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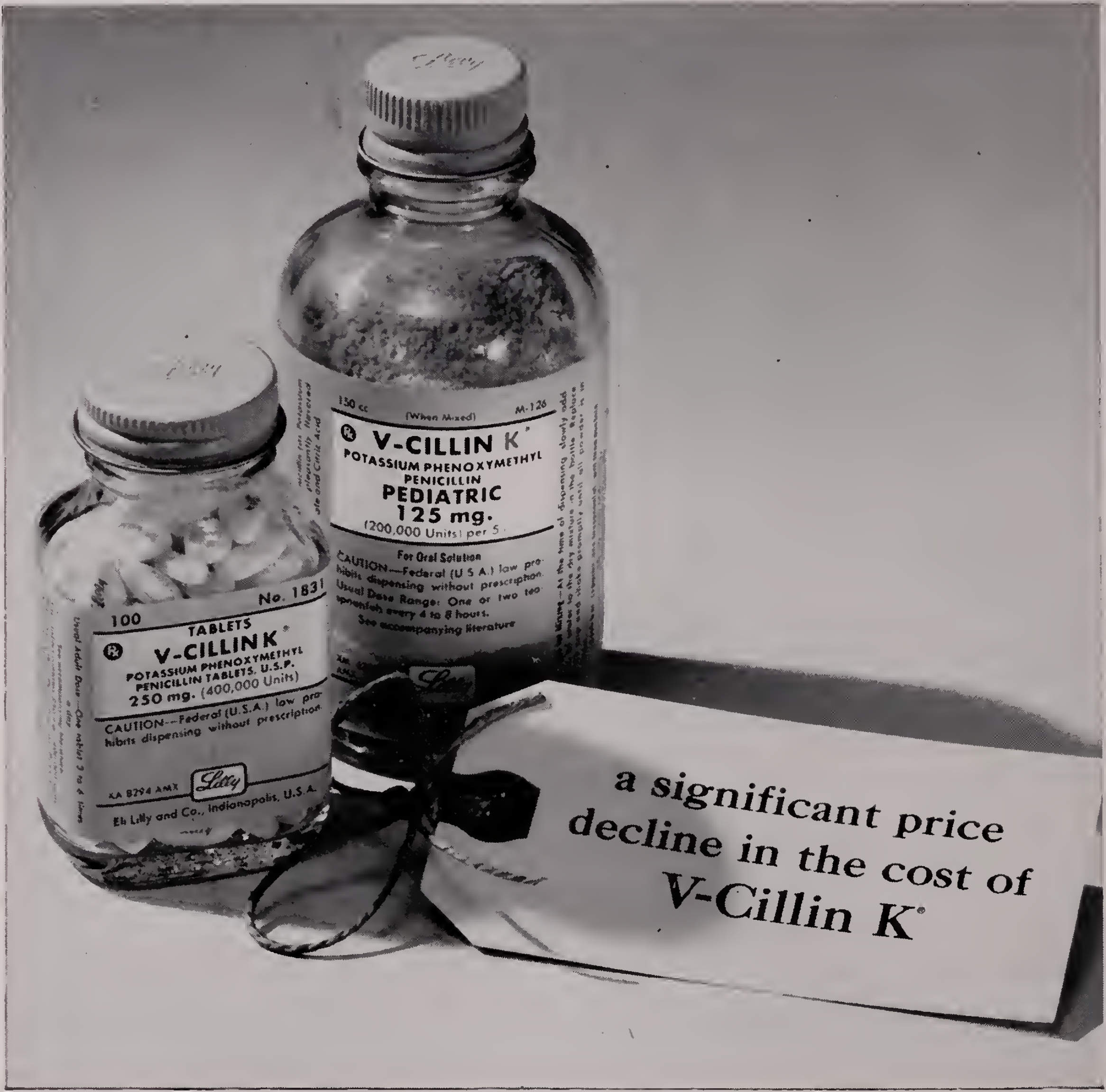
President's Letter

This is the time of year when we get back into full activity. The doctor who is looking for an opportunity to serve his profession in the coming year has unlimited outlets for his interests. Many of them are more or less thrust upon him in his busy life. As the ratio of doctors to population has been decreasing, more and more controls have been established which influence the operation of a physician's practice of medicine. These controls have been created to assure quality medical care by such important groups as the Joint Commission on Hospital Accreditation, the State Department of Health, the City Board of Health, Public Assistance Agencies at the local, state and federal level, Blue Cross and Blue Shield and other carriers, the local hospital council, area-wide hospital planning groups, and medical schools where there is an affiliation. As though conformance with the wishes and regulations of these agencies is not enough, the doctor is expected to reciprocate for staff privileges through service in hospital, clinics or the emergency room, to attend rounds, medical staff meetings, and to be well read in the latest medical developments and to have at his fingertips all information about drug products. In addition, he is expected to participate in research projects and to serve in the hospital on committees such as those for medical records, tissue, and utilization. With all of this he is expected to be a civic leader in his community.

In the local medical society there are offices and committees to be filled. At the state level there are 24 scientific committees ranging alphabetically from The Committee on Aging to the Committee on Rheumatism, the first and last not necessarily being related. There are 21 non-scientific committees concerned with all phases of public relations. In a few weeks the Council and the President of the Minnesota State Medical Association will appoint the committees for the year 1966. It is this committee structure of the Association which I wish to discuss. In most instances the Council and the House of Delegates rely upon the committees for reference and investigation of pertinent subjects. In addition, the committees ought to be a source of thoughtful suggestions for the introduction of new policies and the revision of old ones. Their work is really the life-blood of the Association. The Council and the President, in appointing these committees, try to make them representative and effective by selecting men who have interest and competence in the relative fields. To promote a healthy organization it is desirable to bring in new members each year, while retaining those who have shown interest and ability. There is no better place for a young physician to get started in State Association work. Most of our present leaders have come up through the committees of the local societies and the Minnesota State Medical Association.

While the councilors and the state officers may know of most of those who can be considered for appointment, it is obvious that local initiative on the part of a county medical society or an individual in making candidates known is desirable. Secretaries of the

Continued on page 1386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Some Anatomical Features of the Heart Relative to Normal and Abnormal Function

GEORGE C. RINKER, Ph.D.*
Vermillion, South Dakota

THE HEART OCCUPIES the middle mediastinal region of the thoracic cavity. When the outline of the average heart is projected anteriorly onto the thoracic cage, its base is oriented across the sternum at the level of the third costosternal junction. The upper left margin of the left atrium is seen to present on the upper margin of the third rib at a point somewhat under an inch from the sternal margin (Fig. 1:1); while the junction of the superior vena cava with the right atrium projects on the lower margin of the right third rib about one half inch from the sternal margin (Fig. 1:2). The junction of the inferior vena cava with the atrium is seen to fall behind the chondrosternal junction of the sixth rib (Fig. 1:3). The apex of the heart lies posterior to the fifth intercostal space, just above the margin of the sixth rib, at a point approximately three and one half inches from the ventral midline (Fig. 1:4). The general outline of the heart can be obtained by connecting these points with suitable curved lines. The normal position of the valves of the heart and arterial trunks is also shown. It should be emphasized that the points given are averages and that any individual may show considerable variation from these. There is a rather predictable variation according to general body conformation. In short, broad persons the heart will tend to be more transversely disposed, while in a tall, thin individual it will usually be more vertically oriented. In a normal case, the heart will not occupy more than 50% of the transverse dimension of the thorax.

The base of the heart is relatively fixed by its continuity with the great vessels at the level of the bodies of the fifth to the ninth thoracic vertebra. From the roots of these vessels it hangs suspended in the pericardial sac, "resting" on the anterior slope of the dome of the diaphragm. Orientation of the heart is such that, as seen in the body, the anterior surface consists mainly of the right ventricle and atrium, with only a small area of the left ventricle and the tip of the left atrium visible from this view. The left atrium and ventricle make up most of the posterior aspect of the heart.

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*Department of Anatomy, School of Medicine, University of South Dakota.

The fibrous base or "skeleton" of the heart consists of four dense fibrous rings surrounding the two atrioventricular orifices and the bases of the arterial trunks. These rings give attachment to the fascicles of the myocardium, completely separating the atrial musculature from that of the ventricles. Figure 2 shows schematically the relations of these rings to the major cardiac orifices. From the inner margin of each of the atrioventricular rings thin fibrous sheets extend downward into the ventricles. These, with their endocardial covering form the cusps of the atrioventricular valves (Fig. 2, 3). The fibrous rings supporting the bases of the aortic and pulmonary trunks give attachment to the semilunar valves which guard these exits. Relative positions and terminology of the valves of the heart are shown in Figure 2. For their sternocostal projections refer to Figure 1.

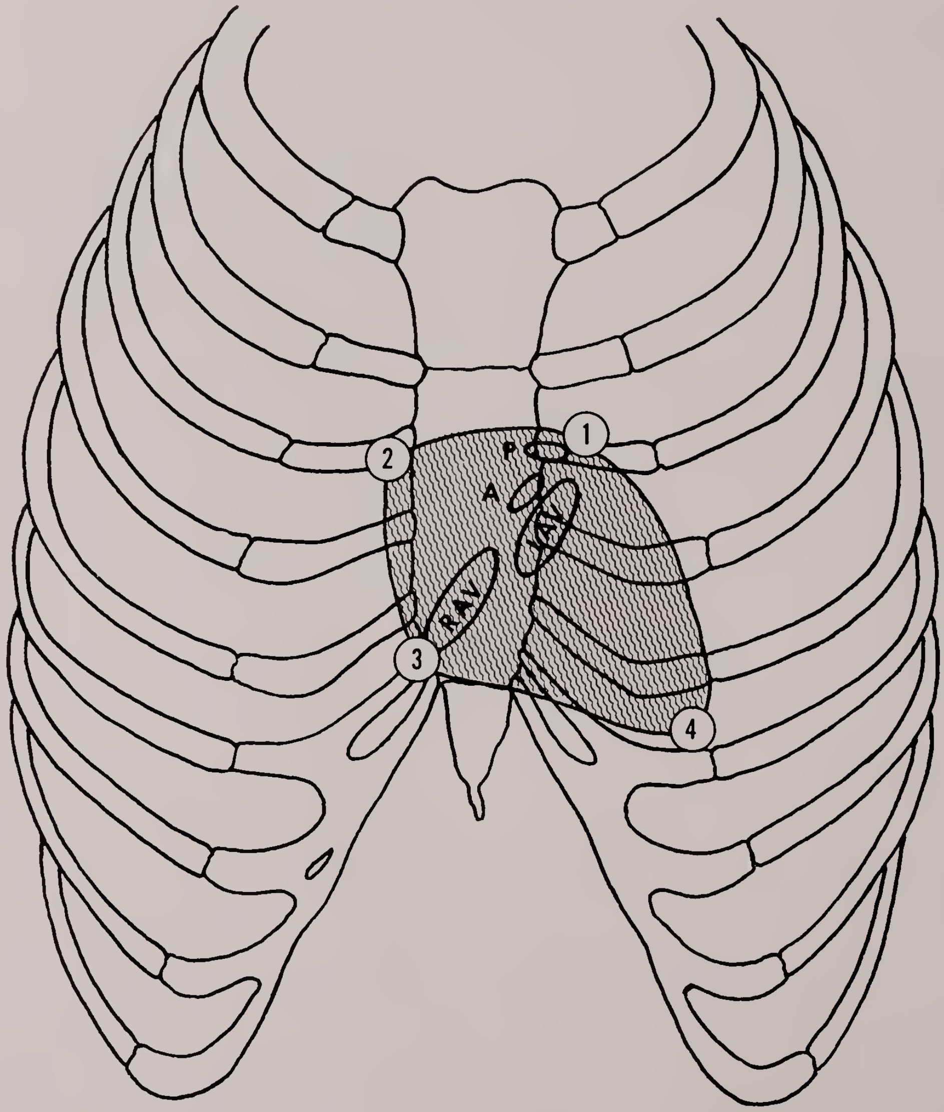

Fig. 1 — Sternocostal projection showing the average location of the heart and its valves. P, pulmonary semilunar valve; A, aortic semilunar valve; RAV, right atrioventricular valve; LAV, left atrioventricular valve.

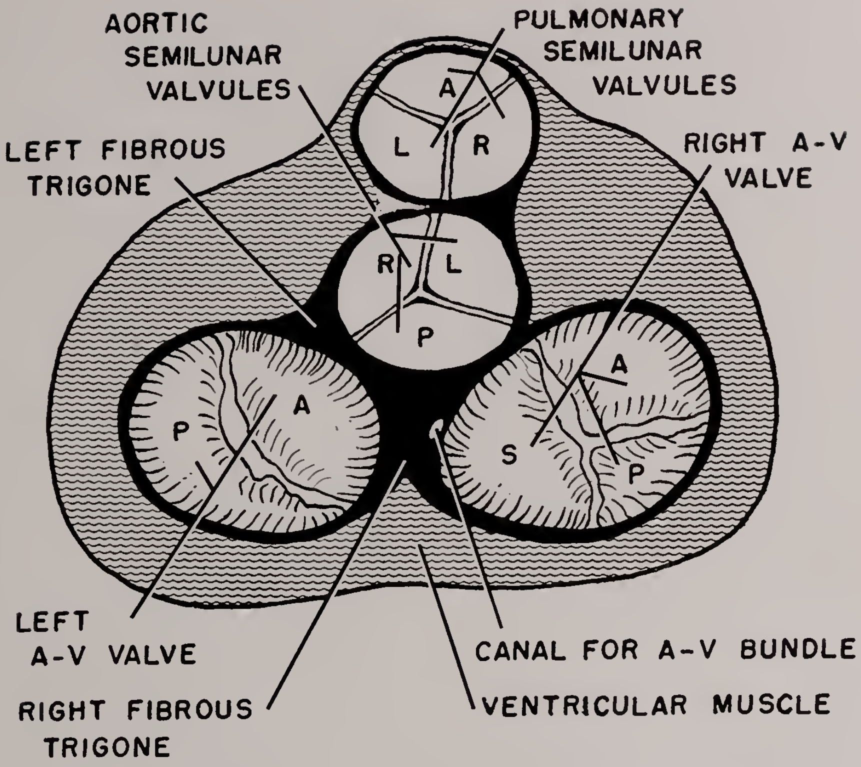
AORTIC SEMILUNAR VALVULES
PULMONARY SEMILUNAR VALVULES
A
L
R
RIGHT A-V VALVE
LEFT FIBROUS TRIGONE
R
L
P
A
P
A
S
P
LEFT A-V VALVE
CANAL FOR A-V BUNDLE
RIGHT FIBROUS TRIGONE
VENTRICULAR MUSCLE

Fig. 2 — Schematic view of the heart with the atria removed, showing relations of valves and fibrous “skeleton” of the heart.

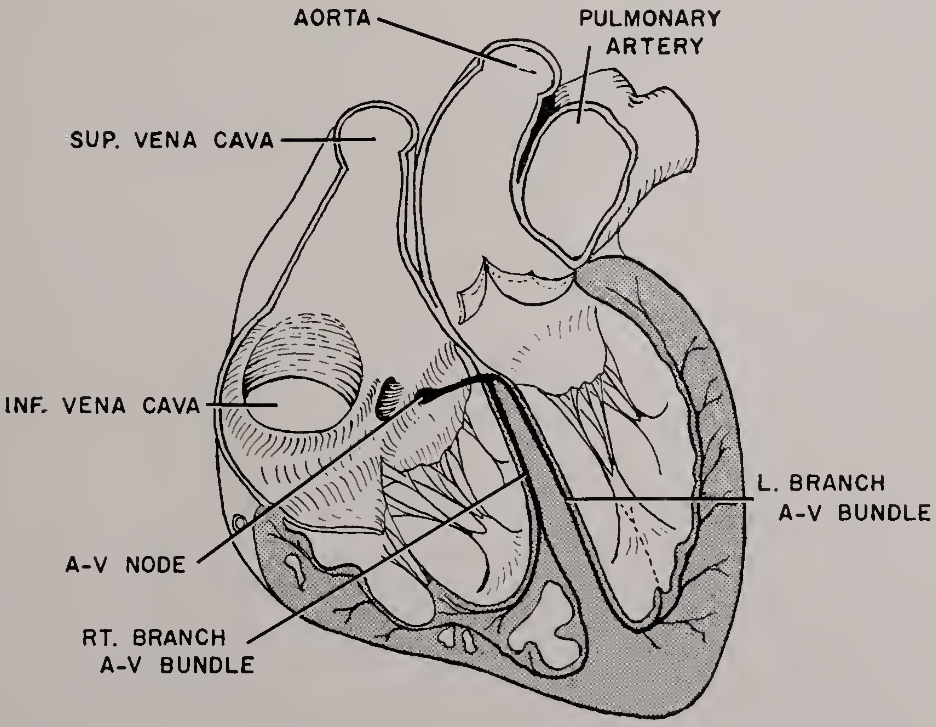
AORTA
PULMONARY ARTERY
SUP. VENA CAVA
INF. VENA CAVA
L. BRANCH A-V BUNDLE
A-V NODE
RT. BRANCH A-V BUNDLE

Fig. 3 — Schematic frontal section of the heart demonstrating relations of the atrioventricular node and bundle.

Blood Supply

Blood supply to the heart is derived from the two coronary arteries.

Right Coronary Artery

The right coronary artery arises from the right anterior aspect of the aorta, emerging from the right aortic sinus. It courses anteriorly, passing at first posterior to the pulmonary trunk, to reach the coronary sulcus in which it runs inferiorly, supplying branches to both the right atrium and ventricle. A branch to the sinoatrial node is given off early in this course. After giving off a rather sizable right marginal branch, the artery continues in the coronary sulcus to the posterior of the heart and turns down in the posterior interventricular sulcus as the posterior interventricular branch.

Left Coronary Artery

The left coronary artery arises from the left aortic sinus and passes anteriorly just to the left of the pulmonary trunk. In the cleft between the pulmonary trunk and the left auricle it divides into its anterior interventricular branch and its circumflex branch. The former passes down the anterior interventricular sulcus, supplying branches to both ventricles. The circumflex branch follows the coronary sulcus around to the posterior of the heart, giving off a prominent left marginal branch, and supplying a large branch to the posterior aspect of the left ventricle.

Venous Drainage

The venous drainage follows a pattern roughly corresponding with that of the arteries. The great cardiac vein originates from tributaries on the anterior aspect of the ventricles and courses upward in the anterior interventricular sulcus, reaching the coronary sulcus in which it runs around the left side, in company with the circumflex branch of the left coronary artery. On the posterior aspect of the heart this vein becomes continuous with the coronary sinus. In its course it receives a left marginal vein and the posterior vein of the left ventricle.

The coronary sinus lies in the posterior atrioventricular sulcus, passing from left to right, and enters the right atrium just to the left of the orifice of the inferior vena cava. Shortly before entering the atrium the coronary sinus receives the middle cardiac vein, which ascends in the posterior interventricular sulcus and the small cardiac vein. The latter vein usually begins on the right margin of the heart, associated with the right marginal artery. It ascends to the coronary sulcus, then runs with the right coronary artery posteriorly and joins the coronary sinus.

A group of three or four anterior cardiac veins is found on the anterior aspect of the right ventricle. These pass upward across the coronary sulcus, emptying directly into the right atrium. The oblique vein of the left atrium, although usually rather small, is of considerable interest in that it is the remnant of the left superior vena cava of the embryo. This vein lies on the posterior aspect of the left atrium in the cleft between the auricle and the left superior pulmonary vein. The site of its junction with the great cardiac vein signals the beginning of the coronary sinus. The oblique vein of the left atrium is continuous with a fibrous strand which attaches at its other end to the left superior intercostal vein. This strand is the ligament of the left superior vena cava. Occasionally obliteration of this system is incomplete, leaving the individual with a functional left superior caval vein.

Venae Cordis Minimae

A system of tiny channels within the musculature of the heart, opening directly into the chambers of the heart, is known as the venae cordis minimae. It would appear that blood flow in these "veins" might well be alternately away from and into the chambers.

Parasympathetic

Nerve Supply

The parasympathetic nerve supply to the heart is derived from the vagus nerves. The preganglionic fibers pass to the heart via the superior and inferior cervical cardiac and thoracic cardiac branches of the vagus on each side. After traversing the cardiac plexuses which lie in relation to the lesser curvature and posterior aspects of the aortic arch, these fibers terminate in synapses with postganglionic neurons which lie in the sulcus between the atria, on the base of the left auricle, and in the walls of the atria. Postganglionic fibers from these neurons end on the musculature of the sinoatrial and atrioventricular nodes.[1] Stimulation of these parasympathetic nerves results in a reduction of force and rate of the heart beat.

Sympathetic

Sympathetic innervation of the heart has its origin in the first five thoracic segments of the spinal cord. The second-order neurons of this system lie in the superior, middle, and inferior cervical sympathetic ganglia, as well as in the first four or five thoracic chain ganglia. Postganglionic fibers pass from all these ganglia to the cardiac plexuses on the aortic arch. Traversing these plexuses, the fibers terminate chiefly in the region of the atria, the sinoatrial node and atrioventricular node, and in relation to the coronary arteries. There is apparently a decided tendency for fibers of both the sympathetic and the parasympathetic systems to distribute principally to the side of the heart corresponding to the side of the body from which they arise. Sympathetic stimulus to the heart results in an increase in the rate and force of the heart beat.

With respect to the effect of the two systems on the coronary vessels conflicting evidence has been presented. It is perhaps most commonly held that vagal stimulation produces constriction and sympathetic stimulation results in dilatation of the coronary arteries. Certain investigators, however, have reported evidence to the contrary.[2]

Afferent Fibers

Considerable numbers of visceral afferent fibers accompany both autonomic pathways to the heart. Those accompanying the vagal branches have their peripheral terminals around the region of the roots of the great vessels. It is generally conceded that these fibers are concerned primarily with cardiac reflexes.

A rich supply of afferent fibers accompanies the sympathetic fibers in the middle and inferior cervical cardiac nerves as well as those fibers arising from the upper four or five thoracic segments of the sympathetic trunk. The cells of origin of these afferent fibers lie in the dorsal root ganglia of the upper five or six thoracic spinal nerves. On the right side, these pass to the sinoatrial node, the atrium and ventricle. Those from the left have their terminals in the walls of the left chambers, the interatrial septum, the pulmonary veins, and the atrioventricular node. The association of these afferents with the upper thoracic nerves accounts for the referral of cardiac pain to regions of the body innervated by these nerves, notably the ulnar aspect of the upper limb and the upper part of the thorax.

Sinoatrial Node

The intrinsic rhythmic activity of the heart muscle is initiated in a small mass of specialized myocardial tissue which lies in the right atrial wall in the cleft between the superior vena cava and the right auricle. The contraction which begins in this sinoatrial node spreads through the atrial musculature, and thus reaches another node of similarly specialized tissue, the *atrioventricular node.* This lies in the interatrial septum just superior and anterior to the opening of the coronary sinus into the right atrium. From this node the contractible impulse is conducted to the ventricular musculature by a neuromuscular bundle, the *atrioventricular bundle.* This bundle of fibers passes through the right atrioventricular fibrous ring (Fig. 2) and runs anteriorly in the upper margin of the muscular interventricular septum (just inferior to the septum membranacea). Here the bundle divides into two branches (Fig. 3), one of which passes down each side of the interventricular septum just under the endothelium. The right branch courses downward, passing in the septomarginal or moderator band to the anterior papillary muscle, distributing to the anterior ventricular muscle. The wide flat left septal branch of the bundle runs downward on the septum, supplying the papillary muscles and general musculature of the left ventricular wall.

In many mammals the atrioventricular bundle is a very discrete, specialized band of tissue with a distinct sheath of connective tissue. In man, however, the bundle is apparently not so definitely specialized. In fact some investigators have failed to demonstrate the presence of specialized fibers at all.[3] Others[4] observed at least a few Purkinje* fibers in over one half of their human specimens. They demonstrated that such fibers in man "have different staining properties, a smaller mean diameter, and variable amounts of myofibrillae." Their conclusion was that these differences accounted for the discrepancies of interpretation by various investigators.

This review is only a brief presentation of the major aspects of cardiac anatomy. If, however, it supports or gives emphasis to the presentations of other contributors which follow, its purpose will have been accomplished.

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*See Test Your Word Score Page 1333.

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Paleopathology IV*

Roentgenographic Data on One Female Mummy

Fourth in Series

Among several Egyptian mummies photographed and studied in detail was that of a woman. Aside from slight but negligible deviations from normality, her head showed a cloudy granulation of the cortex, indicating osteosclerosis due to a healed infection; it also revealed edentia except for five mandibular teeth, probably due to absorptive osteitis.

Her torso and limbs presented no abnormalities except marked kyphosis of the thoracic vertebrae; spondylitis deformans resulting from spinous processes on the mid-dorsal vertebrae and in the lumbar region; partial coalescence of some articular surfaces of the vertebral arches; and evidences of ateriosclerosis in the lumbar ligaments, the rib bodies, the ventral blood vessels of the right scapula, and the radial artery near the wrist.

This lady was doubtless somewhat senile — physiologically if not chronologically.

Illustrations of the roentgenograms of this female mummy with accompanying texts appear in the Anthropological Memoir of the Field Museum of Natural History, Volume III.

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*See Minnesota Med 48:908, 48:1020, and 48:1250, 1965.

The Penalty of Overweight

Whom the gods would destroy they first make opulent — then corpulent.

— **Trumbull Cheer**

At the beginning of a disease choose such remedies as will not lessen the patient's strength. — Rhazes (865-925 A.D.)

Heart Sounds

Simple
and
Yet
Complex

ROBERT L. GRISSOM, M.D.*
Omaha, Nebraska

THE HEART SPEAKS a language to us through its sounds, whenever we listen to it. This language has inflection and pitch; sometimes it sounds ominous and sometimes it seems to jump for joy. Although this language can tell us much, most of us pay little attention to the "lubb-dups," giving preferential attention to the murmurs if they exist. It is my purpose to ignore the murmurs today and to examine each of the familiar heart sounds individually. Also at the bedside we should focus our attention on one sound at a time in order that their language may best be understood by us.

Most physicians will think of only two sounds, the familiar "lubb-dup" in a patient's heart sound findings; but really there are four major sounds, each of which has at least two and some four components. The four sounds may be schematically represented by a diagram[1] as in Figure 1.

The Fourth Heart Sound

Here it can be seen that the fourth sound has both a right atrial and a left atrial component which arise from the tension of the heart wall as atrial contraction forces a final jet of blood into the already distended ventricles. Although regularly seen with sensitive electronic equipment, it is generally inaudible with the ordinary stethoscope. When heard, however, it is a single sound with low frequency and low intensity vibrations of short duration. It can be identified most easily when there is a partial atrioventricular block or a complete heart block. Occasionally in systemic hypertension it may be heard. In one study[2] over 50 per cent of normal persons over 80 years of age had an audible fourth sound. It becomes louder when heart failure is present with an increase in venous pressure and enlargement of the heart. In this circumstance this fourth heart sound will be called an "atrial gallop."

The First Heart Sound

The first sound, which we shall consider next, has been the least understood of all sounds. Normally it is longer in duration and lower in pitch than the second heart sound. Yet this is not always the case. In embryocardia, for example, the first and second sounds are quite similar and the intervals between them approximately the same. In such a circumstance one may find the technique of "inching" down from the base to the apex helpful in timing the heart cycle.

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*Department of Internal Medicine, University of Nebraska College of Medicine, Omaha, Nebraska.

Credit is acknowledged to grant # W-3512-11A, University of Nebraska College of Medicine.

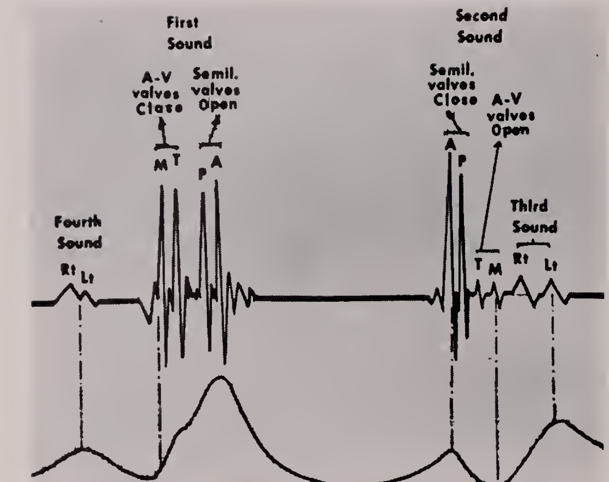


Fig. 1 — From Luisada, by permission. The linear or apex cardiogram, showing only the low frequency impulse, is drawn in the lower trace for reference.

Recent research has revolutionized our interpretation of this sound. Previously most clinicians believed the first heart sound had two principal components, due to closure sequentially of the mitral and tricuspid valves. When splitting occurred it was interpreted as asynchronous closure of these two A-V valves and suggestive of a bundle branch block. There is much evidence now to indicate that the mechanical event of closure of the mitral and tricuspid valves makes up little or none of the first sound. In the experimental dog, for example, the A-V valves have already closed before the rapid vibrations of the first heart sound occur. Intracardiac sound recordings have shown that the majority of the sound vibrations are associated with the rapid rise of pressure in the left ventricle. In the normal heart neither the right ventricle nor the tricuspid valve contributes a great deal to these sounds externally. In most instances in the normal heart the left-sided events precede the right-sided events, although sometimes they coincide. In any case, the very last component can be shown to coincide with ejection into the aorta and pulmonary artery and is principally due to vascular vibrations.

This explanation of the first sound has been dealt with somewhat in detail, since it is possible to confuse initial portions of this sound with a presystolic murmur or to confuse ejection clicks with the fourth component. "Splitting" of the first sound is much less significant as a clinical phenomenon than splitting of the second sound, which will be discussed later. More important than splitting of the first sound is the characteristic "snapping" of the sound of mitral stenosis.

Snapping Sound of Mitral Stenosis.

This has been shown to be due to tension and vibrations of the mitral leaflet and is often a first clue to the examiner that he is dealing with mitral valvular stenosis. Those who do phonocardiograms in preoperative evaluation of mitral disease have found it useful to measure the time from the beginning of the Q wave in the electrocardiogram until the mitral valve closure sound as an index of the severity of mitral stenosis. The longer the interval the "tighter" the stenosis,[3] as a rule.

When there is insufficiency of that valve the first sound progressively diminishes in intensity and may even be "masked" or swallowed up in the murmur. It has been a clinical observation that first-stage A-V block also resulted in a diminished first heart sound, but the best correlation here seems to be myocardial weakness and a slow rise of the intraventricular pressure. Other causes for a prominent first heart sound are anemia, thyrotoxicosis, exercise or increased cardiac output from any cause.

The Second Heart Sound

The second heart sound is generally more admired by clinicians than any other of the sounds. And for good reason! In young persons it is frequently split with inspiration. Much attention is paid to this phenomenon as a teaching device for sophomore medical students in physical diagnosis.

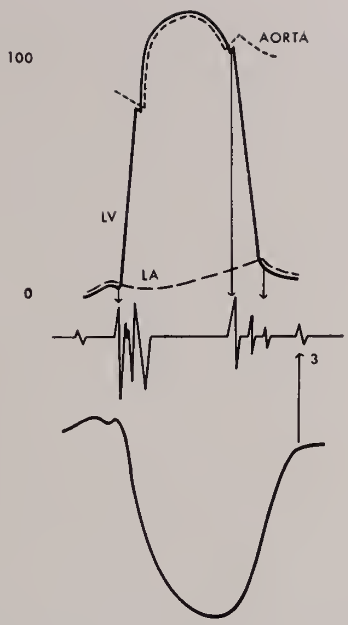
Influence of Inspiration

The second sound splits into the two components when the pulmonary valve closes appreciably after the aortic valve, which it tends to do after inspiration gives an increased right ventricular stroke volume. More blood has been aspirated into the chest and expelled into the pulmonary artery, so that right ventricular systole has been prolonged more than left ventricular systole. Considerable attention has been given to "paradoxical splitting," which, in most cases, is due to unusually late closure of the aortic valve and thus a reversal of the usual relationship. At the same time pulmonic closure, reflecting as it does the duration of right ventricular systole, still lengthens with inspiration and shortens with expiration. Because of its reversed position with respect to the aortic sound, however, the pulmonic closure sound splits from the aortic valve on expiration, not inspiration. This can occur with left-bundle branch block and sometimes in severe aortic stenosis and hypertension.[4] The detection of this gives the doctor who hears it a "one-upmanship" standing.

Pulmonary Component

Close attention ought to be paid to the pulmonary component of this second sound, which is usually best heard in the left second interspace, as an index of pulmonary hypertension. This is the only auscultatory sign of the lesser circuit blood pressure the clinician has and, when loud, is quite reliable for the diagnosis of pulmonary hypertension. It is helpful especially in congenital heart disease and in rheumatic mitral stenosis. Similarly a loud aortic closure sound will best be heard in the right second interspace. It will be loud and sharp in systemic hypertension and in dilatation of the ascending aorta.

Following shortly after this second sound, when there is mitral stenosis, a vibration may often be distinctly heard as the "opening snap" of the mitral valve. It is not listed as one of the "big four" of the heart sounds, but it might well be, since it is a discrete sound and not a murmur. It is shown in Figure 1 as "A-V valves open." The tensing of the valve and its flexibility are important. A skilled examiner can predict from the "sharpness" of the sound whether the valve will be successfully fractured by a "blind" approach at mitral valvotomy. If it is a dull sound, he will predict a less satisfactory result of heart surgery by this technique.



—Time-pressure relationship of the left side of the circulation (above) with time-volume relationship of the left ventricle (below). The third sound occurs at the end of period of rapid filling of the ventricle.*

Fig. 2

In patients with congenital heart disease, the heart sounds have great importance because pulmonary hypertension frequently occurs and produces the loud pulmonary second sound. Also shunts can result in large ventricular flows so that third sounds also are readily heard. One phenomenon that deserves special mention is the "fixed splitting" of the second sound in patients with atrial septal defect. This is a valuable sign. While it may also be found in ventricular septal defect, it is not difficult to distinguish this condition. I have chosen an example to illustrate this by a different means of recording secondary heart sounds, the so-called spectrophonocardiogram. In this type of recording, intensity is reflected by the density of the tracing, and sound frequency by the height. In Figure 3 a double or split second sound[6] is seen in all four areas where it was recorded. This is due to delayed pulmonary closure because of the large right ventricular ejection volume. Although not shown here the splitting was seen regardless of the respiratory cycle and is therefore spoken of as "fixed." The right ventricular flow is so large at all phases that the usual inspiratory increase in flow does not further prolong systole. It is useful to record "fixed splitting" on a phonocardiogram when it is found, but the clinician usually can make the diagnosis of fixed splitting without the recording machine.

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*From Stern, by permission.

The Third Heart Sound

The third heart sound is due to rapid filling of the ventricles and coincides with a filling wave shown in the lower part of Figure 1 as the linear apex cardiogram. This sound may normally be heard in most children but gradually disappears in the young adult, so that it is seldom heard as a physiological phenomenon in the 40s or beyond. When there is heart enlargement, its presence at the same point in the cycle can reliably be interpreted as a ventricular gallop. As such it has ominous significance, often implying heart failure. Also, in marked mitral valve insufficiency when there is a large inrush of blood from the left atrium to the left ventricle, a third sound may be produced. As a gallop sound, however, it usually signifies ventricular dilatation. In the older adult it is often found with arteriosclerotic heart disease in failure. It may be found with anginal pain, only to disappear when the angina leaves. As a low pitched sound, its presence is often missed by the casual observer. Dr. Paul White has shown that it is one of the most significant findings in diseased hearts, yet one that is frequently missed.

Figure 2 will show these sounds[5] plotted against the left ventricular, left atrial and aortic pressure phenomena above the phonocardiographic tracing, with the time-volume relationship of the left ventricle below. A similar diagram could be drawn for the right ventricle with the ventricular systolic pressure levels about one fourth those of the left side. The two sides are so nearly alike in sound production that one illustration serves for both.

In the presence of a tachycardia and heart failure the third and fourth sound "gallops" may be heard as a single set of vibrations known as a "summation" gallop. An illustration of this was shown where the summation gallop was heard when a patient with heart failure was first examined. The next day when the heart rate had slowed, the third and fourth sounds (ventricular and atrial gallops) were heard separately.

The tracing in Figure 3 also shows a systolic click (SC) in the third auscultatory area along the left lower sternal border. Such sounds have no known clinical significance and are thought to arise from the pericardium. Loosely they may be called "systolic gallop" sounds, which is unfortunate because of the serious nature of other gallop sounds. Systolic clicks must also be differ-

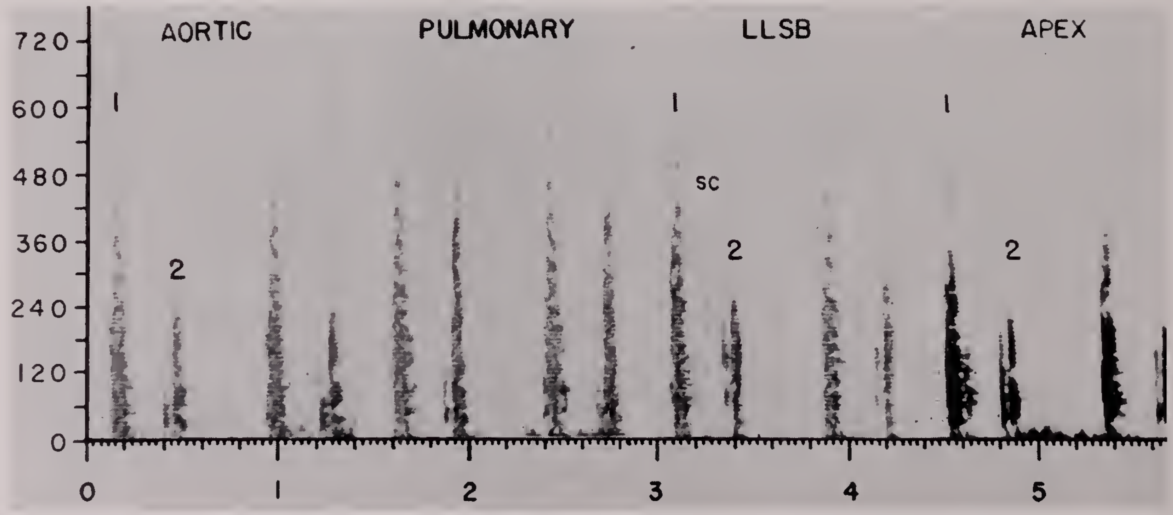

Fig. 3 — The spectral phonocardiogram in a patient with atrial septal defect. The "split" second sound is shown at a constant interval in all locations. The pulmonic closure component is especially loud in the pulmonary area. SC = systolic click. From Stern, by permission.

entiated from "ejection sounds," also called "ejection clicks," which can arise from vibration in a dilated pulmonary artery with the large pulmonary blood flow of an atrial septal defect. Such ejection sounds may also arise in a dilated aortic wall.

Conclusions

This review was intended to show that the heart sounds are no more than simple vibrations of valves or heart walls or the great vessels. Yet they are incompletely understood and for that reason especially are assumed to be complex. Often they yield information more meaningful than murmurs. How else can one simply determine pulmonary arterial hypertension, or a stenotic mitral valve which will respond to valvotomy, or early congestive failure? But the heart sounds must be sought out individually in the patient and studied carefully. It is interesting to hear their language too. And they will speak much more clearly to us if only we will listen to what they have to say.

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IT'S THE LAW

Settlement Reported in Cardiac-Arrest Case

A settlement in the total amount of $300,000 has been reported in a case in which a hospital in Nassau County, New York, a surgeon, and an anesthesiologist were charged with negligence in the care of a ten-year-old boy who suffered a cardiac arrest. The arrest occurred following surgery while the patient was in the hospital recovery room.

It is reported that the boy is a permanent invalid, suffering mental retardation, loss of vision, and cerebral palsy. It was contended that the surgeon and the anesthesiologist were negligent in not remaining with the patient in the recovery room and in failing to make sure that the recovery room was properly equipped and staffed. It was also alleged that the hospital was negligent in failing to maintain an adequate recovery room and to enforce proper rules for the conduct of surgical procedures, and that the nurse, who was alone in the recovery room, was inexperienced and failed to detect the cardiac arrest for several minutes.

(News Release, Manhasset, N. Y., December, 1964.)

Despotism can no more exist in a nation until the liberty of the press be destroyed, than the night can happen before the sun is set. — Colton

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Mom says: The heritage of disciplined privation makes you wealthy with little.
— C. O. R.

Ventricular

THE NATURE of the heart's rhythmical action has aroused man's interest for centuries. According to Scherf and Schott[1] arrhythmical activity of the heart had been noted as far back as the sixth century B.C. Until the end of the last century discussions of the cardiac arrhythmias were largely descriptive in nature, and inferences about the significance of the arrhythmias were speculative. Due largely to Engelmann's[2] significant work in 1895 on the refractory period and compensatory pause, understanding of the physiology of arrhythmias reached a level applicable to clinical interpretation and resulted in attempts at classification.

Present interpretation classifies abnormal cardiac rhythms into two broad categories: (1) disturbances in impulse conduction, and (2) disturbances in impulse formation. In the latter category, abnormal impulses may arise in the atria, the A-V node and bundle, or in the ventricles. Recurrence of such abnormal impulses constitutes an abnormal rhythm. Such rhythms may be *passive* (arising as a result of depression of the sinus pacemaker), or they may be *active* (arising as a result of an ectopic focus of impulse formation). The present discussion is concerned only with those arrhythmias designated as active, when some local condition exists which serves to initiate an abnormal impulse. It is generally agreed that the local conditions which initiate abnormal impulses affect one or the other of the two basic properties of the heart: irritability and rhythmicity.

Enhanced Rhythmicity as a Factor in Ventricular Arrhythmias

The property of rhythmicity is especially well developed in the sinus venosus node which acts as the pacemaker of the heart.[3] Intracellular recordings have shown that in cells of the sinus venosus node a slow diastolic depolarization takes place.[4] When the depolarization reaches a critical threshold potential a propagated action potential is initiated which spreads over the entire heart. Most attempts to explain the spontaneous depolarization of pacemaker cells have been based on the Hodgkin concept of membrane permeabilities.[5] As suggested by Weidmann,[6] diastolic depolarization could be due to a decrease in potassium permeability, to an increase in sodium permeability or to a reduction in the activity of the sodium pump (see later). In any event, diastolic depolarization represents an alteration of the cell membrane such that sodium leaks into the fiber. The critical threshold potential is the value at which the sodium inward current exceeds the outward diffusion of potassium, resulting in a sudden and complete depolarization.

It is plausible to explain some forms of ventricular arrhythmia on the basis of an

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Arrhythmias*

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enhancement of rhythmicity, i.e., an ectopic focus in the ventricle where local changes act to periodically depolarize the cell membrane and initiate an independent automatic rhythm. That the ventricular tissue has inherent rhythmicity is implied in the observation of Patten and Kramer[7] on the embryonic chick heart. In their preparation, the first heart beat began in the ventricular tissue. This pacemaker activity was subsequently taken over by the more rapid atria and then by the S-A node (sinus venosus) as development proceeded. Hecht[8] also shows, in his Figure 15 recorded at high speed, a small diastolic depolarization in frog ventricular fibers suggesting that pacemaker activity is a normal though latent property of ventricular fibers. Enhancement of latent rhythmicity could account for ventricular extrasystoles, although Hoffman and Cranefield[9] state that they have never observed pacemaker activity in ventricular fibers (dogs) even during ventricular fibrillation. Nevertheless, it is probable that in the experimental preparations, irritability is more prone to be affected than is latent rhythmicity. Therefore, it is not surprising that pacemaker activity is not encountered in ventricular intracellular recordings. Pacemaker activity is regularly observed in Purkinje fibers,[6] and Katz[10] is of the opinion that all ventricular extrasystoles arise from terminal Purkinje network fibers. Certainly enhanced rhythmicity of ventricular fibers should give independent ectopic rhythms with rates of 30 to 40 per minute. Di Palma and Schultz[11] point out the necessity for this slow rate. In rare instances this does occur (parasystole), in which an independent pacemaker in the ventricle exists with the normal sinus pacemaker. The beats due to the ectopic pacemaker become manifest when they fall on nonrefractory ventricular tissue. These ectopic beats would, therefore, occur in various phases of the cardiac cycle and bear no relation to the sinus beat. When they occur at the same time as the sinus beat, they may fuse with the normal beat.

Influence of Calcium

The reason for development of enhanced rhythmicity is conjectural and no real explanation can be offered. However, calcium deficiency is known to favor automatic impulse formation,[12] and local changes in calcium may be involved. Also, some observations made by Burn[13] on the synthesis of acetylcholine by heart tissue and the relation of the cellular concentration of acetylcholine to automatic impulse formation may have a direct bearing on development of ectopic pacemaker in cardiac tissue. It is difficult to explain, as Kaufmann and Rothberger[14] pointed out in 1920, how the ectopic center is protected from depolarization by the more frequent sinus venosus nodal impulse. Nevertheless, such directional blocks do exist normally in the conduction tissue, as when ventricular extrasystoles are prevented from activating the atria. The physiology of this phenomenon is coming under close scrutiny and an answer may be forthcoming.

Altered Irritability as a Factor in Ventricular Arrhythmias

Unlike the independent rhythm of parasystole, the more common arrhythmias are those in which the ectopic beat follows the preceding beat at a constant and fixed interval. The preceding beat initiates the abnormal beat. The abnormal beat is therefore, a passive phenomenon, the "forced" contraction of Lewis,[15] and a true premature ventricular contraction. In support of this is an interesting experiment by Goldenberg and Rothberger[16] in which an arrhythmia with coupling was produced in dogs by the intravenous injection of strophanthin combined with inhalation of a mixture of 30 per cent CO_2 in O_2.

Vagal stimulation produced cardiac standstill. No ventricular beats occurred. Had an independent rhythm existed in the ventricle it should have persisted during vagal stimulation. Scherf[17] did a similar experiment in rabbits with the same results, showing that each premature contraction was precipitated by and dependent upon the preceding beat. There are two main theories advanced to explain the mechanism underlying premature contractions with fixed coupling: (1) origin of the impulse in an ectopic focus of high excitability, and (2) origin of the impulse by re-entry into an island of previously depressed tissue. Both mechanisms depend on the preceding beat for their existence.

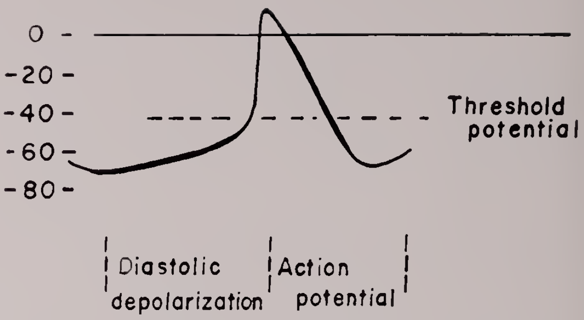


Fig. 1 — The action potential of pacemaker fibers of the S-A node, showing slow diastolic depolarization which, when reaching a critical threshold potential, initiates a propagated action potential.

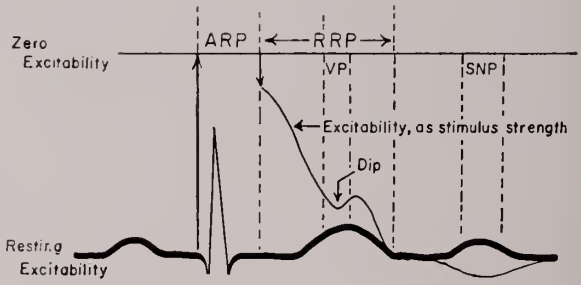
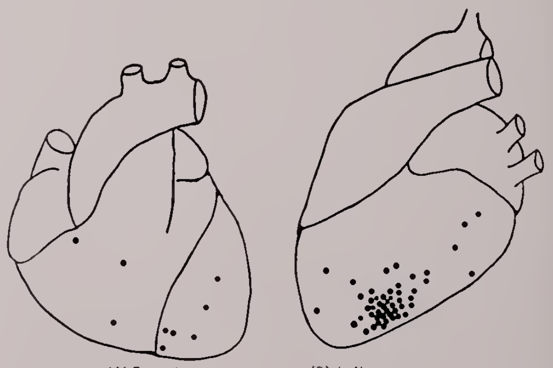


Fig. 2 — Representation of the excitability of heart muscle during one cardiac cycle. The ECG isoelectric line is plotted on the line representing resting excitability. During inscription of the QRS (depolarization) the excitability decreases to zero. Thereafter, recovery returns gradually. Excitability curve is drawn as the stimulus strength necessary to excite. The recovery period may be followed by a period of supernormality. ARP-absolute refractory period. RRP-relative refractory period. VP-vulnerable period. SNP-supernormal period.



(A) Frontal view (B) Left view

Fig. 3 — Drawing of a dog heart in the frontal and left view on which are plotted the origin of all epinephrine-induced ventricular premature contractions found in 59 trials on 14 dogs. There is a concentration of ectopic beats arising in the posterior aspect of the left ventricle near the apex.

Supernormal Phase — U Wave

The essential feature of the former is that the premature contraction is generated in an ectopic focus where local changes from the preceding impulse produce a temporary rise in excitability. That such a rise in excitability is possible was demonstrated by Adrian[18] in 1920 for frog heart. It is called the supernormal period, and Adrian noted that it is accentuated by acid or fatigue. Hoff and Nahum[19] demonstrated a supernormal period in mammalian ventricle (cat) under barbiturate anesthesia. The supernormal phase corresponds to the U wave of the electrocardiogram and, according to Nahum and Hoff,[20] is the period when most premature ventricular contractions occur. Lepeschkin[21] has brought together much evidence relating the U wave of the surface electrocardiogram to the supernormal phase of ventricular excitability and to the initiation of coupled premature contractions. He finds that factors which increase the amplitude of the U wave facilitate the appearance of coupled premature contractions: epinephrine, digitalis, calcium, hypopotassemia, acidosis. Scherf and Schott[7] offer a mild objection to the view that the supernormal period is responsible for initiating ventricular premature contractions, at least the common variety with fixed coupling, on the grounds that such a period cannot be regularly demonstrated in all hearts. Wolferth[22] also raised a similar objection. In addition, application of veretrine, which prolongs the negative afterpotential (the supernormal period) and precipitates ectopic beats, does not always produce fixed coupling. Lepeschkin[21] also notes that quinidine suppresses coupled extrasystoles, yet at the same time increases the U wave (supernormal period). While these objections are valid and must enter into any argument relating the supernormal period to coupled premature contractions, much can be said in favor of the supernormal period as providing a focus for initiation of premature contractions.

Of some relevance to this problem are some experiments performed in our own laboratory. We wished to decide whether a ventricular premature contraction arose from a specific and predictable focus in the ventricle. In order to test this, spatial vectocardiograms of the dog, one from the frontal plane and one from the sagittal plane, were visualized on separate oscilloscopes and the tracings photographed simultaneously. The vector loops were enlarged and transposed to the sides of a large plastic box ruled in coordinates. This allowed us to locate the origin of the ventricular complex. The procedure was carried out a total of 59 times in 14 dogs. Figure 3 illustrates the points of origin of all ventricular premature contractions. The majority originated in a circumscribed area of the left ventricle, posteriorly near the apex. We attempted to explain why premature contractions arose from this circumscribed area of the left ventricle. Plastic casts of the arterial tree showed no deficiency of coronary blood flow to this area. Chemical determination showed no difference in epinephrine, norepinephrine or total catecholamine content. There was a slight difference in the isethionic-acid level, but this was of questionable significance. Of some relevance to the results is the fact that this area corresponds to the point of attachment of the large papillary muscle of the left ventricle, and electrocardiograms showed that the ventricular premature contractions arose during the inscription of the U wave.

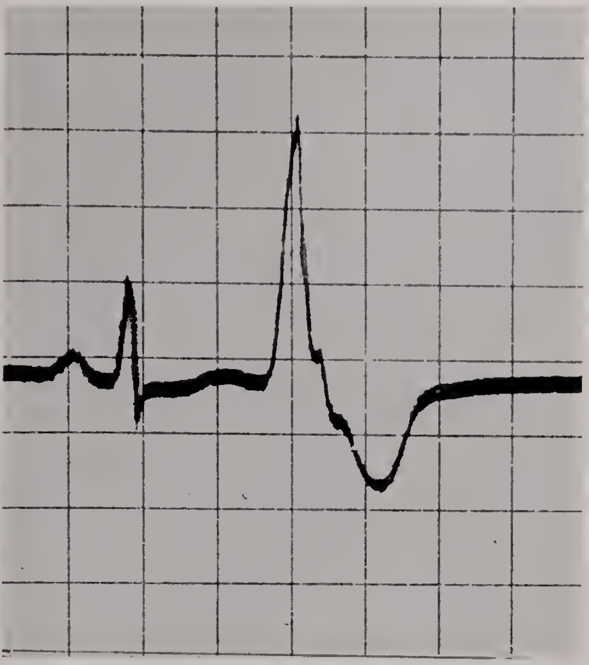


Fig. 4 — Ventricular premature contraction arising from the U wave. Record taken from a 60-year-old male with some indication of ischemia of the left ventricular wall.

Influence of Stretching

The observation of Dudel and Trautwein[23] indicates that stretching increases the negative after-potential of cardiac muscle. Therefore, as Lepeschin[21] points out, the negative after-potential (supernormal period, U wave) would be expected to be highest in parts of the ventricle subjected to greatest stretch. The papillary muscles bear the entire systolic ventricular pressure that is exerted on the atrioventricular valves. Indeed, Furbett et al.[24] noted that the U waves are most

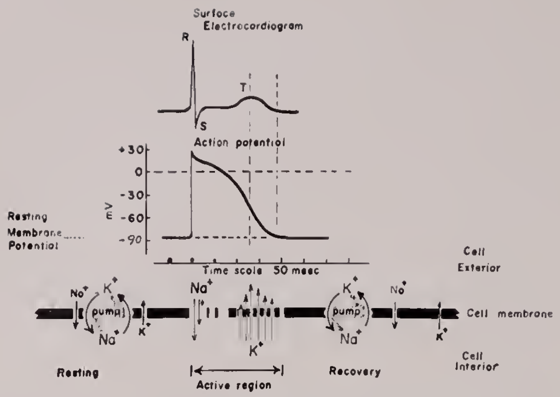


Fig. 5 — Schematic representation of the mechanism responsible for the membrane resting and action potential denoting the ion movements responsible for the electrical variation. At the top, the surface electrocardiogram is drawn in relation to a cell-action potential. During depolarization Na+ moves into the cell and during repolarization K+ moves out of the cell.

prominent on the ventricular surface opposite the insertion of the papillary muscles. Increase of the supernormal phase of ventricular repolarization due to stretching would appear to be a reasonable explanation for the origin of ventricular premature contractions in the small circumscribed area defined in our experiments. Indeed, stretch or distention of the cardiac chambers during hypertension or congestive heart failure is a common cause of cardiac arrhythmias.[25]

Depressed Heart

It is an important observation that coupled arrhythmias also develop in hearts which are depressed. A re-entry mechanism is offered to explain such coupled rhythms. This mechanism predicts that islands of cells exist in which recovery is slower than normal. The normal impulse passes around the depressed area but re-enters it at a later time in recovery, i.e., when the island of tissue has sufficiently recovered to permit entry. The re-entry then serves as a locus for initiation of a second beat. In 1940 Wiggers and Wegria[26] reported that single induction shocks applied during the vulnerable period (that period just preceding the peak of the T wave[27]) could, depending on the strength of the shock, produce single or multiple premature contractions or fibrillation. Hoffman et al.[28] relate the vulnerable period to the major dip in the recovery curve, and Brooks et al.[29] explain the vulnerability of the ventricle during this stage of recovery as due to the prolonged recovery of a localized area which allows for re-entry of the normal impulse. It seems that factors which depress the heart may produce localized areas of depression with prolonged refractory periods or decreased conduction allowing for re-entry and development of coupled beats.

Ions in Ventricular Arrhythmias

Inasmuch as premature contractions seem to develop during the recovery (repolarization) phase of myocardial activity, it is pertinent to inquire into those events which are happening during this time. The irritable property of the heart cell is dependent upon the functional characteristics of the cell membrane. The functional properties of the membrane have been deduced through an explanation of the mechanism underlying three fundamental observations. *First,* the cell membrane separates extracellular fluid of high sodium (Na^+) and low potassium (K^+) from an intracellular fluid of high K^+ and low Na^+. *Second,* Na^+ and K^+ are continuously diffusing into and out of the cell, i.e., the cell membrane is slightly permeable to Na^+ and K^+, and more so to K^+ than to Na^+. *Third,* an electrical potential of 80 to 90 millivolts exists across the cell membrane of the resting cell, with the inside of the cell negative to the outside. The reversal of the electrical potential difference across the cell membrane during activity produces the "action potential." The present concept of resting and membrane action potential is summarized in Figure 5.

Sodium-Potassium Transport Mechanism

The bold dark line represents the cell membrane. This membrane is slightly permeable to Na^+ and K^+, and more so to K^+ than to Na^+. In the resting membrane, as Na^+ diffuses into the cell it is actively transported to the outside by means of a special Na^+ transport mechanism located in the membrane. As Na^+ and K^+ diffuse into the cell and Na^+ is actively extruded, this leaves an accumulation of K^+ inside the cell. The rising concentration of K^+ inside the cell forces K^+ to diffuse away from this high concentration to the outside of the cell, leaving a residual negative charge behind on the inner surface of the membrane. When the residual negativity pulling K^+ into the cell is equal to the force of the K^+ concentration tending to force K^+ out of the cell, there is no *net* movement of K^+; although K^+ is constantly moving into and out of the cell. The resting membrane potential is determined by the ratio of the K concentration and is negligibly affected by the Na concentration. Figure 5 depicts extrusion of $Na^+ - K^+$ exchange pump. The action potential (moving from right to left) represents a sudden reversal of electrical sign (a change from 80 to 90 mV inside negative to 20 to 40 mV inside positive) due to a sudden and large increase in membrane permeability to Na^+, and Na^+ moves into the cell. A plateau near zero potential (slow repolarization) follows, at the end of which the electrical potential rapidly reverts to the resting level (rapid repolarization) due to an increase in the membrane permeability to K^+, and K^+ moves from the inside of the cell to the outside. During the action potential the cell has gained a small amount of Na^+ and lost a small amount of K^+. The $Na^+ - K^+$ pump then extrudes the Na^+ gained during depolarization and reclaims the K^+ lost during repolarization.

Inasmuch as ventricular premature contractions develop during the repolarization phase of myocardial activity, it is reasonable to relate such arrhythmias to the efflux of K^+ which occurs at this time. The apparent relationship of myocardial potassium loss to cardiac arrhythmias is well documented, and potassium administration is known to suppress ventricular arrhythmias. The arrhythmias accompanying toxic doses of the digitalis glycosides apparently are related to the large loss of K^+.

Influence of Taurine

In our own laboratory we were able to show that the compound taurine (2-aminoethanesulfonic acid) prevented the loss of cell K^+ from heart slices incubated in the presence of "toxic" amounts of epinephrine or digoxin.[30] Indeed, the presence of taurine caused an accumulation of cell potassium (Table 1).

We were interested in determining whether the effect of taurine in restricting K^+ loss from heart slices would be effective in suppressing epinephrine or digitoxin-induced ventricular arrhythmias in the intact dog heart. Acute experiments performed on anesthetized, vagotomized dogs showed that taurine was effective in suppressing the premature ventricular contractions caused by adequate doses of epinephrine. Additional experiments showed that taurine was effective in abolishing the cardiac arrhythmias produced by either acute or prolonged chronic administration of digitoxin.[31] Figure 6 is a record from this series. Taurine appeared

TABLE 1

Effect of Taurine on the Intracellular Potassium Content of Dog-Heart Slices

Experimental Condition	Intracellular K mEq/λ cell H_2O
Control (18)[a]	144 ± 0.08[b]
Epinephrine, 10^{-4}M (12)	139 ± 1.24
Taurine, 10^{-4}M plus epinephrine 10^{-4}M (9)	163 ± 0.85
Digoxin. 1.25 X 10^{-4}M (8)	139 ± 0.72
Taurine, 10^{-4}M plus digoxin, 1.25 X 10^{-4}M (8)	153 ± 1.31

[a] The figures in parentheses show the number of individual determinations

[b] Standard error of the mean

Data from Welty and Read, J Pharmacol Exp Ther 144:110, 1964.

TABLE 2

Effect of Taurine and Chemically Related Compounds on the Dose of Digoxin Required to Produce Arrhythmias

Compounds adjusted to pH 7.4 infused at constant dose of 3.3 μM/kg/min.	Total dose of digoxin required to produce arrhythmias when injected in a constant amount of 1 μg/kg/min.
	μg/kg
Control	119 ± 3.7
Taurine (2-aminoethanesulfonic acid)	180 ± 5.3
3-Aminopropanesulfonic acid	150 ± 9.0
Ethanesulfonic Acid	143 ± 8.4
Ethylamine	136 ± 7.5
Sulfanilic Acid	120 ± 4.6

to be the most effective of several chemically related compounds in protecting the heart against digoxin-induced arrhythmias. Table 2 gives the results of acute experiments in which test compounds were administered intravenously at the same time as the toxic dose of digoxin (as judged by runs of premature contractions). While ethanesulfonic acid and ethylamine raised the toxic dose of digoxin, both compounds were ineffective in reverting an established digoxin-induced arrhythmia to a normal sinus rhythm, whereas both taurine and 3-aminopropane were effective. Additional work on intact, anesthetized dogs showed that taurine prevented the large efflux of potassium from the heart which accompanies large doses of epinephrine[30] (Figure 6).

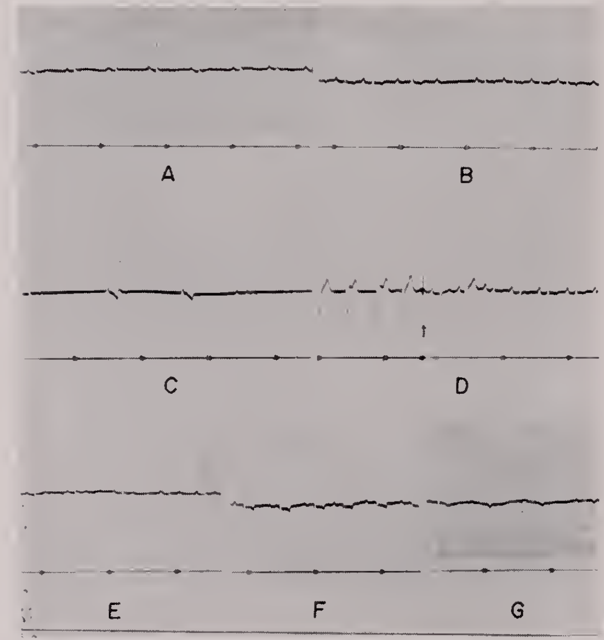


Fig 6 — Sections of the electrocardiogram (Lead II) to demonstrate the effect of taurine in inhibiting toxic manifestations of chronic administration of digitalis in trained, unanesthetized dogs. In this dog a total of 732 μg of digitoxin (chrystodigin, Lilly) had been administered orally over 29 days. A — control before digitoxin administration. B — 25 days of digitoxin administration, showing prolonged P-R interval, beginning A-V dissociation. C — three hours after B, showing complete A-V dissociation. D — 29 days of digoxin administration, premature contractions. At the arrow, 10 m mole of taurine per kg. was administered i.v. over a 30 min. period. Conversion to a normal sinus rhythm begins in about 5 min., when short runs of normal rhythm appear, and is virtually complete in 15 min.
E, F and G are 2 hours, 24 hours and 30 days after taurine. Chart speed 25 mm. per sec. Standardization 1 mV = 5 mm. (From Read and Welty, Rev Canad Biol Symp 1965).

Antiarrhythmic Drugs

The antiarrhythmic drugs, quinidine, procaine amide and sympathomimetic amines operate to retard the potassium efflux* which precedes cardiac arrhythmias. Quinidine appears to depress K efflux,[32] although the effect may be secondary to a depression of inward Na movement.[33] Gold and Carday[34] proposed the use of vasopressor agents in cardiac arrhythmias and suggested that the antiarrhythmic property was due to their ability to maintain coronary blood flow. However, Robertson and Peyser[35] showed that small doses (less than 5 μg/kg) of epinephrine increase the intracellular K^+ of myocardial cells (confirmed by Wadell).[36] Stafford,[37] in a detailed study, also showed that adrenalin (2 X 10^{-8}M) increased the uptake of K in the spontaneously beating

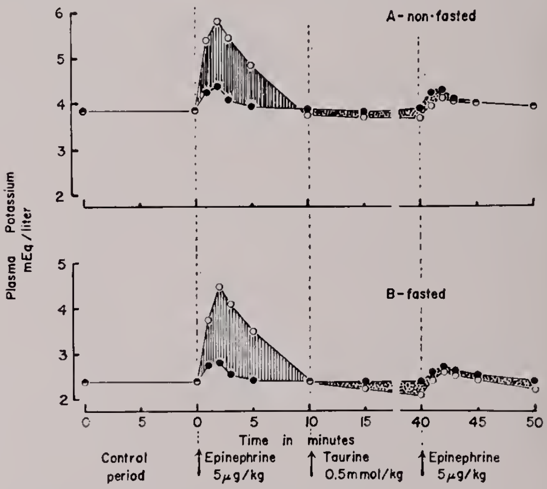


Fig. 7 — Plasma K levels of blood simultaneously drawn from the coronary sinus and the arch of the aorta in nonfasted and 12-hour-fasted dogs. Note the difference in the K levels during the control period of nonfasted and fasted dogs. Intravenous injections were made at the times indicated by the arrows. The cross-hatched area represents loss of K^+ from the heart; the stippled area represents uptake of K^+ by the heart. Taurine administration prevented the egress of K which accompanies adequate doses of epinephrine. Immediately following epinephrine, there is a rapid uptake of K^+ by the heart followed by an efflux. The uptake is not shown due to the spacing of the samples (From Read and Welty, Rev Canad Biol Symp 1965).

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*See Test Your Word Score Page 1333.

auricles. In intact dogs in which the coronary sinus blood is continuously monitored, we have consistently observed that 1 μg of epinephrine per kg. causes an uptake of myocardial potassium. Reasoning that epinephrine should block K^+ egress, Regan et al.[38] reported that a sustained infusion of epinephrine in intact dogs prevented the arrhythmias due to strophanthidin. These authors felt that the antiarrhythmic property was related to the prevention of myocardial potassium loss and not to an effect on arterial pressure and coronary blood flow.

All of the antiarrhythmic drugs are known to have important side effects, and potassium administration is not without hazard. It is possible that taurine, a nontoxic and natural substance in the heart, may prove effective in the control of digitalis intoxication and in certain forms of ventricular arrhythmias.

Summary

Ventricular arrhythmias may be produced by two basic mechanisms: development of an ectopic focus of impulse formation and re-entry into an area of depressed conduction. Ventricular arrhythmias are commonly associated with those phases of repolarization corresponding to the supernormal phase (U wave of electrocardiogram) or terminal part of the relative refractory period (T wave of electrocardiogram). Such arrhythmias are correlated with a large myocardial potassium loss. Substances which restrict myocardial potassium loss appear to be effective agents in suppressing ventricular arrhythmias. Taurine, a nontoxic and natural substance in the heart, appears to have antiarrhythmic properties due to its ability to retard myocardial potassium loss.

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7-38 May be obtained from the author or the reprints.

FANCONI'S SYNDROME

This syndrome may include a wide variety of birth anomalies and it is thought that the disorder is probably transmitted as a Mendelian recessive trait. It is associated with hematologic and renal metabolic disturbances, including osteomalacia, pseudofractures, hypophosphatemia, renal glycosuria, and ameno-aciduria.

There may be hypoplasia of the bone marrow, anemia, leukopenia, thrombocytopenia, and ecchymosis or hemorrhage may occur in the mucous membrane.

Alterations in the blood chemistry consist of increased renal secretion of amino-acids, increased renal phosphate clearance with hyperphosphaturia, renal glycosuria and high urinary ammonia.

The chronic organic acidosis which results is thought to be from an inborn error of protein metabolism with an associated abnormal function of the proximal convoluted renal tubules and a failure to reabsorb glucose, phosphate, amino-acids, bicarbonates, potassium and uric acids.

The treatment consists of measures designed to correct the electrolyte imbalance, the administration of large doses of vitamin D, high intake of calcium and phosphorus, by the administration of alkalinizing mixtures of potassium chloride, sodium citrate and citric acid.

Durham — Encyclopedia of Medical Syndromes.

Cardiac Muscle

the Ultrastructure

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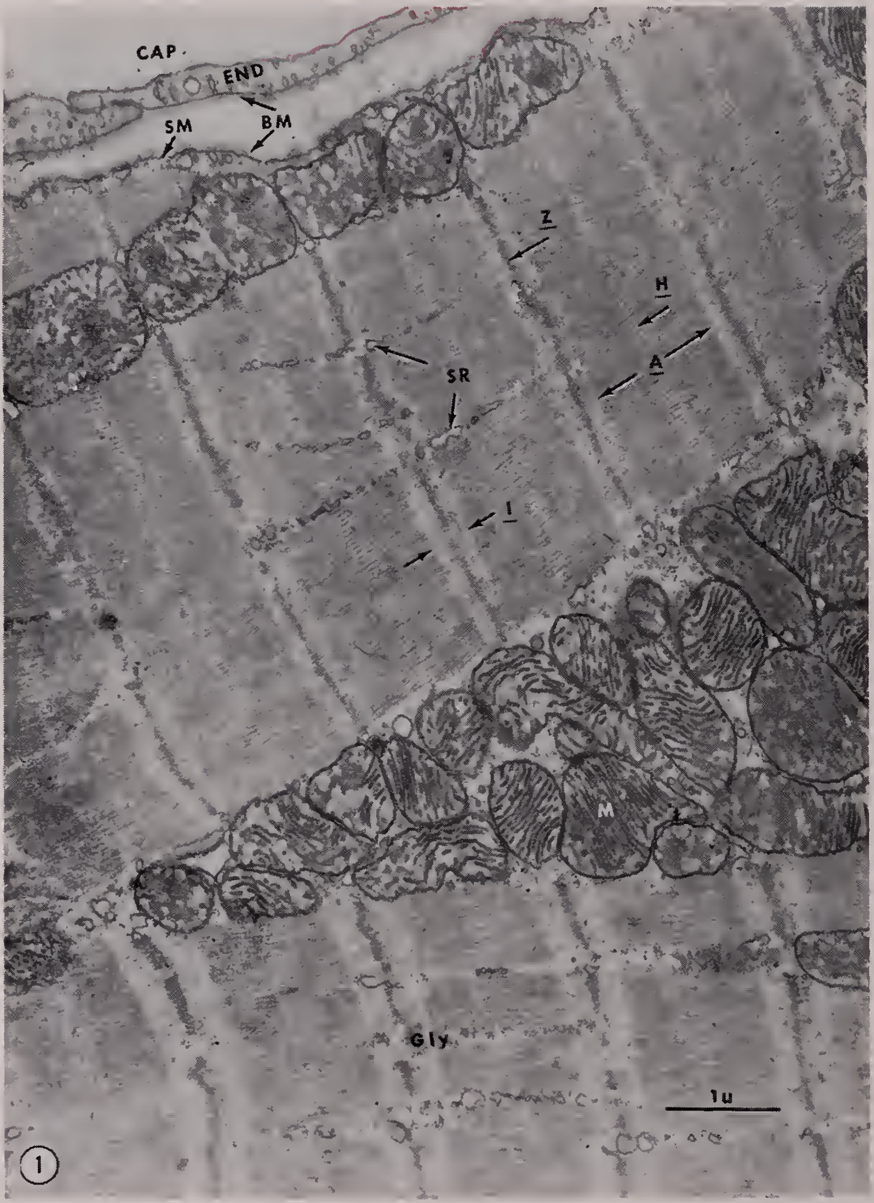

Fig. 1 — Electron micrograph of a longitudinal section of rat cardiac muscle. Lead citrate stain, X20,000. *CAP*, capillary; *END*, endothelium; *SM*, sarcolemma; *BM*, basement membrane; *SR*, sarcoplasmic reticulum; *GLY*, glycogen; *M*, mitochondria; *A*, A-band; *I*, I-band; *H*, H-band; *Z*, Z-line.

STUDIES OF THE ultrastructure of cardiac muscle in man, the dog and the rat have shown that, in general, the basic organization and morphology are similar to those of skeletal muscle.[1,2] Variations in structure from that of skeletal muscle, other than the presence of intercalated discs and branching fibers, are related to the fact that cardiac muscle fibers must contract frequently and simultaneously, with but short recovery periods.

Myofibrillae

In ultrathin longitudinal section (Figure 1) the fibers are seen to be composed of closely packed myofibrillae which are cross-banded in register. In electron micrographs, the anisotropic A-bands are dark, having a narrow, light zone, the H-band, at the mid-region. Adjacent to the A-band is a light isotropic zone, referred to as the I-band, each of which is transected by a dark Z-line. A sarcomere is described as the portion of a myofibril which is included between two successive Z-lines. In studies of the ultrastructure of skeletal muscle, it has been shown that the banding (anisotropic and isotropic areas) results from longitudinally oriented, interdigitating thick and thin filaments.[3-5] The thick filaments, averaging 100 Å in diameter, are located in the center of the sarcomere and are composed of myosin. In relaxed muscle, these filaments traverse the A-band and the H-band. The thin filaments are composed of actin, averaging 50 Å in diameter. They originate at the Z-line, traverse the I-band extending through the A-band just to the H-band. In skeletal muscle, cross-bridges between the actin and myosin filaments in the A-band have been described,[3] but these have not been particularly evident in cardiac muscle.

Filaments

In transverse sections, under high magnification, two types of filaments can be observed, and the arrangement and pattern of the filaments in different areas of the sarcomere are discernible (Figure 2). A section passing through an A-band shows the hexagonal arrangement of the thick myosin filaments, between which the orderly pattern of the less dense, thin actin filaments are located (Figure 2, encircled). A section through the H-band reveals only thick myosin filaments in orderly arrangement; a section through an I-band shows only thin actin filaments in a less orderly pattern (Figure 2).

The sarcolemma is double-layered, characteristic of plasma membrane, and is invested with a basement membrane. Numerous micropinocytotic vesicles are usually present. The cytoplasm of the fibrillae is homogeneous and contains, between fibrils, numerous, randomly distributed, electron-dense granules which have been interpreted as being composed of glycogen (Figure 1).

Heart muscle contains a complex membranous vesicular system investing the myofibrillae. This system, termed the "sarcoplasmic reticulum,"[6] is located between the myofibrillae and is composed of a system of tubules running parallel to, and transversely around them. At intervals, usually at the Z-line and the H-bands, the tubules coalesce into sacs forming winding transverse channels. An additional separate transverse tubule system, smaller in diameter than the sarcoplasmic reticulum, is also present at the Z-line. This separate system has been termed the "T-system." Together, the systems of tubules, i.e., the organization of the sarcoplasmic reticulum and the T-system, are referred to as the "triad" and are considered to be an ideal means for rapid communication and distribution of the action potentials necessary for excitation and contraction.

The mitochondrial content of cardiac muscle is extremely high as compared to skeletal muscle. These organelles are located beneath the sarcolemma and between the myofibrillae. They have no particular relationship to any region or portion of the fibrils or to the tubule system. Structurally, they are similar to mitochondria in other cells, being bounded by a double membrane, the inner layer of

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which is transversely infolded to form cristae. Frequently the cristae are arranged spirally. The large number of mitochondria in heart muscle is a reflection of the high metabolic demands necessary for the continuous activity of this tissue.

Intercalated Discs

The intercalated discs, so characteristic of cardiac muscle, have been shown to consist of two specialized cytomembrane interfaces of adjacent muscle cells in the position of the Z-band.[7] The interfaces of the intercalated disc are separated along their entire winding length by a variable space, with no continuity of fibrils across this intercellular gap. Some portions appear as two apposed cell membranes without unusual differentiation (Figure 3, star), but specialized modifications are commonly present. Scattered irregularly along the disc are structural alterations resembling the form of desmosomes,* having cytomembranes of increased density and dense material in the adjacent cytoplasm (Figure 3, triangle). Another type of modification of the interface also occurs. This

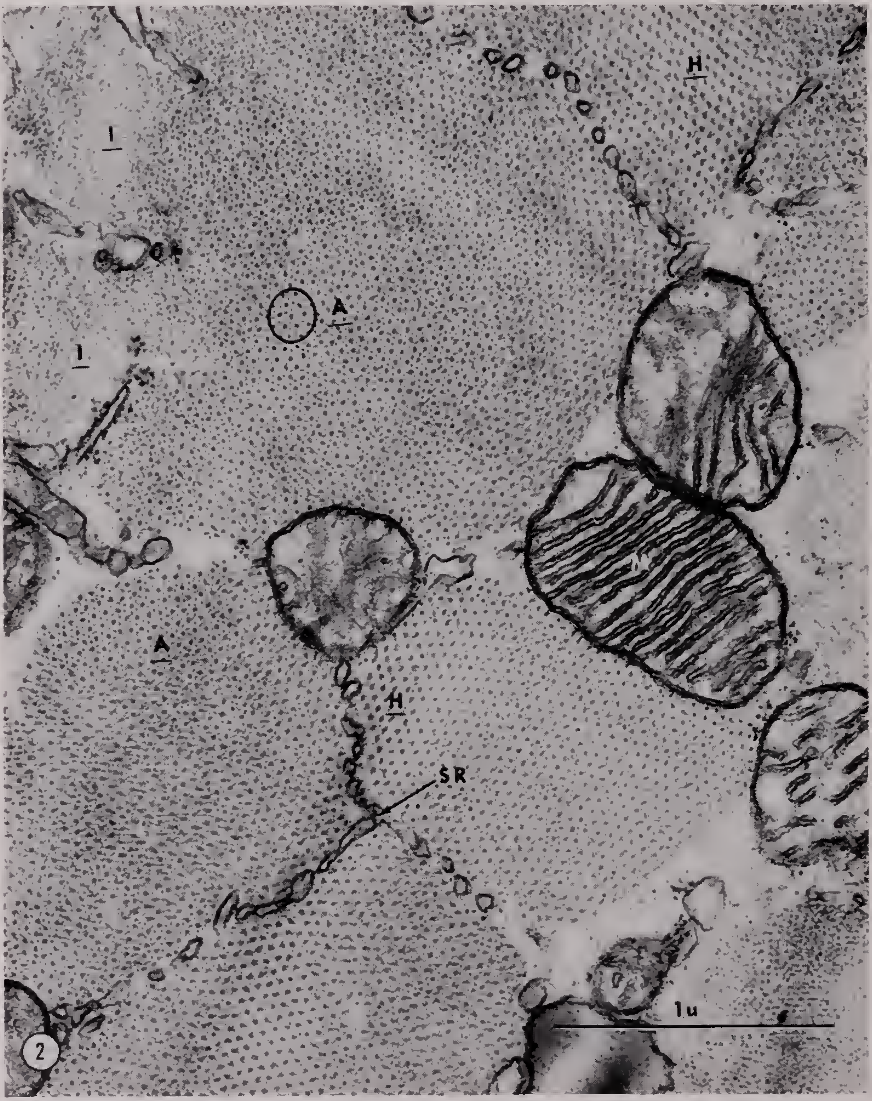

Fig. 2 — Electron micrograph of a transverse section of rat cardiac muscle. Lead citrate stain, X51,000. *CIRCLE*, hexagonal arrangement of myosin fibrils in A-band; *SR*, sarcoplasmic reticulum; *M*, mitochondria; *A*, *I*, *H* refer to sectioning through respective bands.

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*See Test Your Word Score Page 1333.

form appears as a very dense area of the cytomembrane, but without dense material in the adjacent cytoplasm and with a reduction in the width of the intercellular space, having the interfaces in regular close apposition, about 100 Å (Figure 3, spot).

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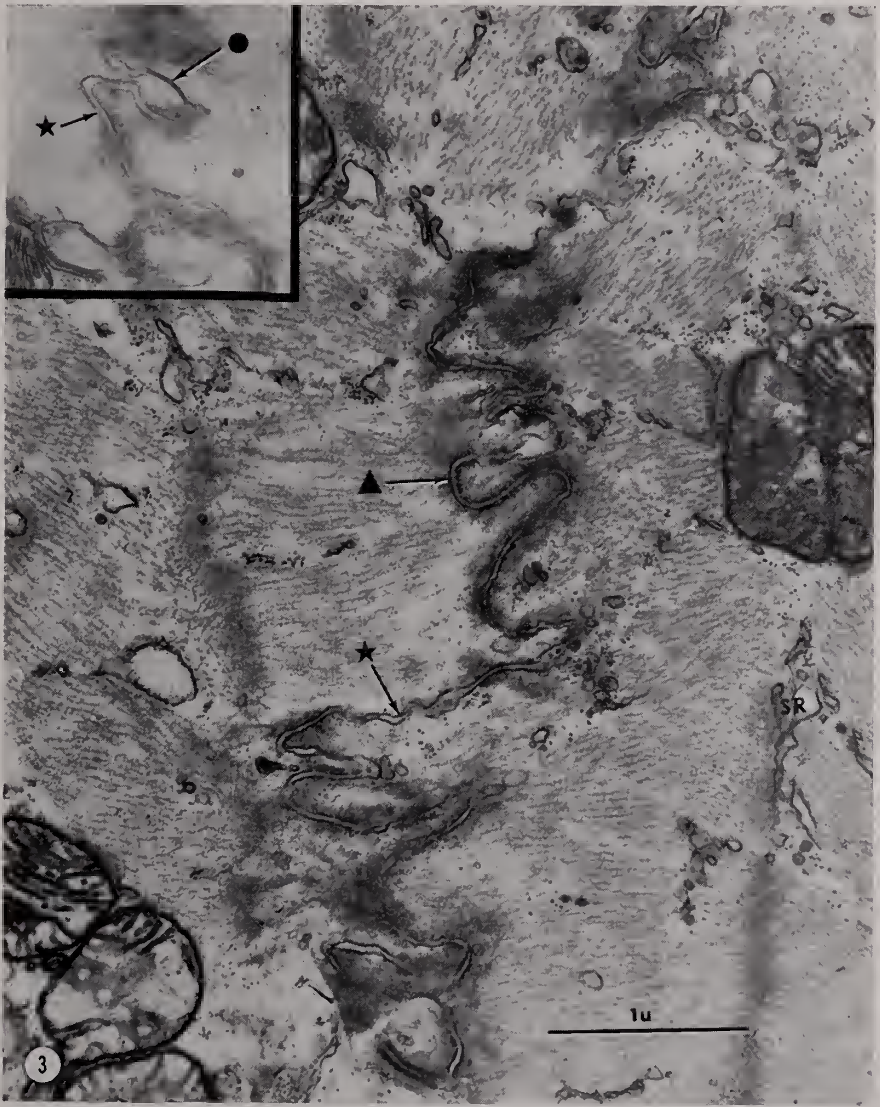

Fig. 3 — Electron micrograph of intercalated disc in rat cardiac muscle. Lead citrate stain, X36,000. *STAR, TRIANGLE, SPOT* indicate three variation in appearance of intercalated disc. See text. *SR*, sarcoplasmic reticulum.

Heart Diagnostics in Ancient Egypt

The Scribe of the ancient Egyptian Papyrus dealing with medicine was evidently cognizant of the physiological-emotional reactions of the human heart. He appears to have been sure of himself; neither incertitude nor inhibition is detectable in his naive and rather touching exposition:

> When Anger arises in his Heart, behold it is a seething-up of the parts of the Intestine and the Liver. His Ear is on the alert, his vessels fall after their rising heat has dissolved everything.
>
> When the Heart is sad, behold it is the moroseness of the Heart, or the vessels of the Heart are closed up in so far as they are not recognizable under thy hand. They grow full of Air and Water.
>
> When the Heart feels an aversion, behold it is the Bitterness of the Heart because of Inflammation in the Anus. Thou findest it big and something forms itself in his Abdomen as in his Eye.
>
> When his Heart spreads out, behold the vessels of the Heart are with excrement.
>
> When the Heart is sick, behold there is an Oppression of the Heart, or it is an Overflow of Blood which arises in the Heart. It falls down and approaches his diaphragm, while his Heart feels an aversion.
>
> When his Heart is in its right place the Fat of the Heart is on the left side. It neither rises upwards nor falls downwards. It remains soundly in its place.
>
> When his Heart trembles and there is much fat under his Left breast, behold it is his Heart which causes a little of the sinking because his disease is spreading.
>
> When dryness befalls his Heart, behold it is the dryness of Fire that befalls it. He sighs often and his Heart is eaten up with anger; this is because his Heart is full of Blood, which in turn is due to drinking Warm Water and eating Bad Food.
>
> When his Heart is afflicted and has tasted sadness, behold his Heart is closed in and darkness is in his body because of anger which is eating up his Heart.
>
> When it is Fate that he shall go Up-on-High, behold it is his Heart which determines that he shall go Up-on-High.*

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*Bryan, Cyril: The Papyrus Ebers, D. Appleton and Company, New York, 1931, p. 126-131.

Astrology & Medicine

The planets Jupiter and Venus are benefics unless so aspected that their otherwise favorable influence is voided. Strongly afflicted, Jupiter disposes to circulatory disorders, pleurisy, diabetes, and obesity; Venus to throat affections, lymphatic ailments, and venereal diseases.

During October Jupiter is morning star and Venus evening star.

Electrolyte Alterations in Cardiac Disorders*

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TABLE I
Distribution of Body Fluids

	% of body weight	liters per 70 kg. man
Extracellular	20	14
Blood Plasma	5	3.5
Interstitial Fluid	15	10.5
Extracellular	50	35

THE HUMAN BODY consists of some 70% water, which is distributed in the several compartments as indicated in Table 1.

Body-Water Balance

The level of body fluids is regulated quite closely by the balance between fluid intake (actual fluid, fluid content of solid foods and metabolic water produced in the combustion of foodstuffs) and fluid loss (evaporation from the lungs or skin and renal or fecal excretion). Ordinarily, *excess fluid intake* leads to a decrease in osmotic pressure of the plasma and increased renal flow with production of a dilute urine. *Decreased fluid intake* or excessive extrarenal fluid loss leads to dehydration, decrease in salivary secretion, drying of the pharyngeal mucosa and thirst. Secretion of the antidiuretic hormone by the pituitary contributes to the conservation of water in this condition. Ordinarily, the satisfying of thirst controls the total body fluid.

Influencing Factors

In addition to the role of the kidney and pituitary body in regulating total fluid volume, the renal conservation of electrolytes is mediated by the adrenal hormones, particularly aldosterone, which controls the tubular reabsorption of sodium in exchange for excreted potassium and hydrogen ion. The net result of osmotic and electrolyte regulation is a rather accurately controlled homeostasis with the stable milieu interne of Claude Bernard reflecting in its composition the probable analysis of sea water at the time when the early vertebrates moved from the marine to the fresh-water environment.

The constancy of distribution of fluids between the several compartments listed in Table 1 depends on the factors controlling the secretion of lymph and its reabsorption.

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Fundamentally, secretion of lymph and its reabsorption depend on the colloidal osmotic pressure of plasma (oncotic pressure) in relation to the hydrostatic pressure of the circulating blood, as indicated by the following equation relating to the capillaries:

(secretory pressure) = (blood pressure) — (oncotic pressure)

To demonstrate the relationship diagrammatically, Figure 1 illustrates the equilibrium in a tissue capillary, the numerical figures being somewhat arbitrary.

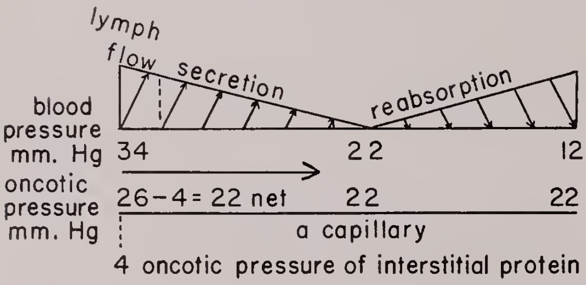

Fig. 1 — Normal Secretion of Lymph.

Renal Edema

In the case of renal edema, in the nephrotic syndrome, the loss of plasma albumin lowers the colloidal osmotic pressure of plasma, shifting the point of no secretion to the right and increasing the excess of secretion beyond what can be removed by the normal lymph flow, the excess remaining in the tissue spaces as edema. In congestive heart failure, accumulation of fluid in the capillaries leads to both dilation and ischemia of the tissue capillaries with increased permeability for protein. With increased protein in the tissue spaces, the net colloidal osmotic pressure is reduced. Due to congestion, blood pressure in the capillaries is increased. Both these factors increase the secretory pressure, with resulting edema as indicated in Figure 2, the numerical figures being arbitrary.

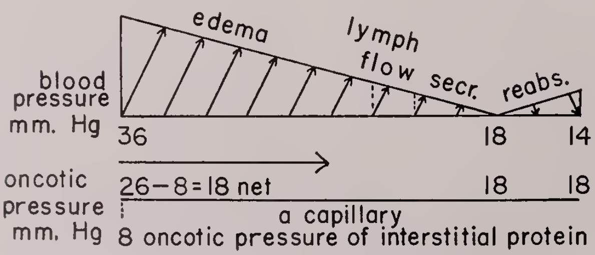

Fig. 2 — Edema in Congestive Heart Failure.

Backward Failure

In a recent symposium, Streeten[1] has reviewed the theories of backward and forward failure as they apply to congestive heart failure. Hoffman[2] has also presented the rationale of these two concepts, which are not mutually exclusive.

According to the backward-failure concept, the stretched myocardial fibers no longer allow complete emptying of the heart on systole, so that an excess of blood accumulates behind the heart, increasing the venous pressure back to the venous end of the capillaries, leading to increased transudation of lymph as indicated in Figure 2. The accumulation of fluid in the tissue spaces, which can take place without the supplying of additional salt, leads to a hypovolemia in the intravascular fluids and an increase in fluid intake, diluting the plasma and stimulating secretion of vasopressin by the action of osmoreceptors in the diencephalon.

The intermediation of "volume"[3] or "stretch" receptors, whose localization is not definite but has been variously assigned to the hypothalamus, aorta, carotid, atria, the great veins, the central arteries or to the kidney itself, may, by a mechanism which is independent of the hypophysis, cause an increase in aldosterone, which tends to increase the retention of sodium, favoring the retention of the edema, which develops insidiously and rapidly with a hyponatremic plasma. Because of the intravascular hypovolemia and hyponatremia, the delivery of the edema is difficult, requiring use of the mercurial diuretics.

Forward Failure

The forward-failure concept is based on a diminution of cardiac output, so that the pressure and volume of blood in the great arteries are low, with the result that the "volume" or "stretch" receptors postulated above are presumed to increase the production of aldosterone, with the same results as occur in the backward-failure concept, but with the additional result of a decrease in renal plasma flow and glomerular filtration. The tubular activity would still be near normal, so that a large reabsorption of sodium chloride and water would be expected to produce an eventual engorgement of the capillary and venous circulation with simultaneous edema. In this concept there is the additional factor of a greater degree of competence in the right heart than in the left (which is usually the site of failure), so that more blood is delivered to the smaller (5% of vascular volume[4]) pulmonary bed than to the larger (55% of vascular volume) systemic bed, with resultant pulmonary congestion and dyspnea with rapid shallow breathing.

Left Ventricular Failure

Left ventricular failure results in decreased blood flow through nearly all the regions of the body with a correspondingly greater extraction of oxygen from the slowly moving blood and a lowering of the venous oxygen reserve. Because of restricted blood flow through skeletal muscle, fatigue and weakness may be symptoms.[5]

Right Ventricular Failure

Conversely, when there is right ventricular failure, general systemic venous congestion and peripheral edema are prominent, with obvious engorgement of the liver, spleen, splanchnic bed and skin. Elevated venous pressure with distention of the veins, peripheral edema and ascites are obvious symptoms.

Treatment Rationale

It has been pointed out by Maxwell and Kleeman[6] that the increased vasopressin and aldosterone in congestive heart failure not only promote reabsorption of water and sodium chloride, but that aldosterone promotes the tubular loss of hydrogen ion and potassium in exchange for the sodium retained, significantly reducing the cellular potassium reserves. Increased vasopressin results in water conservation with production of hyponatremic enema,* in which the serum potassium may be either high or low. The obvious rationale of treatment is the early promotion of diuresis by mercurial diuretics, digitalization, and the eventual use of a low-salt diet with the chlorothiazide type of diuretics. In view of the fact that there is frequently depletion of potassium and chloride, it is usually necessary to administer oral potassium chloride. During the period of early treatment, while edema is being delivered and digitalization accomplished, serum electrolyte analysis, particularly sodium and potassium, is a useful adjunct to rational treatment.

With the recent emphasis on the role of increased vasopressin (antidiuretic hormone) on the retention of water, and of aldosterone on the reabsorption of sodium at the expense of lost potassium, the hyponatremic edema of chronic congestive heart failure has been visualized by Takasu et al.[7] in terms of the osmolar clearance and water clearance[8] under conditions of water loading and water deprivation. The osmolar clearance is the milliosmols excreted per minute, the ratio of osmolarity of urine to osmolarity of plasma multiplied by the ml. of urine excreted per minute.

$$C_{osm} = \frac{U_{osm}}{P_{osm}}. V$$

The free-water clearance is obtained by subtracting the osmolar clearance from the volume of urine per minute. The result may be positive for urines more dilute than blood plasma or negative for urines more concentrated than blood plasma.

$$C_{H_2O} = V - C_{osm}$$

The free-water clearance in congestive heart failure is less responsive to a water load, remaining lower than normal responses, and the osmolar clearance does not rise to its normal height during a subsequent fluid restriction period. Takasu et al.[7] recognize several groups in which the hyponatremia of chronic congestive heart failure is due to:

1. Low setting of the osmoreceptors controlling secretion of the antidiuretic hormone. These patients excreted large amounts of free water on water loading but remained hyponatremic, although the urine osmolarity increased during the ensuing water-deprivation period.
2. Glomerulotubular imbalance with lowered glomerular filtration and normal

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*See Test Your Word Score Page 1333.

tubular secretion. These patients maintained a relatively low and constant osmolar clearance and water clearance, unaffected by the intake or deprivation of water. A portion of these showed delayed water clearance, the response occurring during the nocturnal fluid restriction period.

3. A combination of glomerulotubular imbalance and a low setting of the osmoreceptors. These patients excreted the water-load fluid during the night rather than at the time when water was administered.

Summary

The regulation of water and sodium content of blood plasma are under the regulatory control of vasopressin (antidiuretic hormone) and aldosterone respectively. In congestive heart failure, hyponatremic edema is a regular finding, induced by an increased secretion of vasopressin (antidiuretic hormone) under the influence of osmoreceptors in the diencephalon, which retains water, and an increase in aldosterone under the influence of as yet vaguely understood "volume" or "stretch" receptors. The hyponatremic edema requires mercurial diuretics to start delivery of the edema, followed by digitalization and cholorothiazide type diuretics for control.

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Progress

"I've tried all the medical faculty: they can diagnose beautifully, they have the whole of your disease at their finger-tips, but they've no idea how to cure you. There was an enthusiastic little student here, 'You may die,' said he, 'but you'll know perfectly what disease you are dying of!' And then what a way they have of sending people to specialists. 'We only diagnose,' they say, 'but go to such-and-such a specialist, he'll cure you.' The old doctor who used to cure all sorts of disease has completely disappeared, I assure you, now there are only specialists and they all advertise in the newspapers. If anything is wrong with your nose, they send you to Paris: there, they say, is a European specialist who cures noses. If you go to Paris, he'll look at your nose; I can only cure your right nostril, he'll tell you, for I don't cure the left nostril, that's not my specialty, but go to Vienna, there there's a specialist who will cure your left nostril. What are you going to do? I fell back on popular remedies."

— Fyodor Dostoyevsky, The Brothers Karamazov, 1880

If I am wrong, the sooner I am knocked on the head and annihilated so much the better. — Charles Darwin

The Chemistry
of
Congestive Heart Failure*

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NORMAL FUNCTION of the heart depends upon the rhythmic, coordinated, sequential contraction of its parts. Failure of rhythmic excitation, abnormalities of excitability, or loss of contractility give rise to impaired function.

Types of Congestive Heart Failure

It is an important generalization that congestive heart failure occurs when the load imposed upon the heart exceeds the capacity of the heart for work. Olson and Schwartz[1] have suggested that congestive heart failure can be divided biochemically and hemodynamically into two forms: high-output metabolic failure and low-output nonmetabolic failure.

High-Output Metabolic Failure

In high-output metabolic failure, factors such as anemia, thyrotoxicosis, beri beri, etc. interfere with energy production in the cardiac muscle and are responsible for the ultimate failure of the myocardium. In severe anemia or anoxia the oxidative enzymes of the Krebs cycle and electron transport do not function and deteriorate rapidly following periods of relative anoxia. These changes are associated with fragmentation of the normal ultra-structure of the myocardial sarcosomes. Studies have shown that the decline in work capacity associated with anoxia is proportional to the decline in phosphocreatine content and later to a fall in adenosinetriphosphate (ATP) concentration. Myocardial failure resulting from hormonal imbalances such as thyrotoxicosis is also due to a defect in free energy production. In this case the oxygen consumption is highly elevated, but there is over-all low cardiac efficiency. The myocardial stores of ATP and phosphocreatine are exhausted, a condition related to the blockage of oxidative phosphorylation by thyroxin. Failures such as those seen in beri beri are related to a lack of the coenzyme thiamine, resulting in a depletion of cocarboxylase. This coenzyme is concerned with the conversion of pyruvate to acetyl coenzyme A; thus the oxidation of carbohydrates cannot proceed to completion — with resultant loss of energy.

Low-Output Nonmetabolic Failure

Energy production appears to be preserved in low-output nonmetabolic failure. According to Wollenberger[2] failure occurs because of an inability of the myocardium to utilize the energy produced. The metabolic behavior of the failing heart in dogs subjected to cardiac valvular surgery (producing chronic low-output congestive heart failure) revealed

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that in comparison to normal dogs, the cardiac output was decreased, but coronary blood flow and myocardial oxygen consumption were normal. Rossi and Dianzani[3] could demonstrate no defect in oxidative phosphorylation and indeed found the level of high-energy phosphate compounds to be normal in low-output failure. Studies using the dog heart-lung preparation, open and closed-chest dog experiments, and human subjects, have shown that glycolytic enzymes of the cytoplasm, the dehydrogenases, and the electron transport chain of the sarcosomes function normally.

Influence of Oxygen

It has been suggested in the past that anoxia within the hypertrophied cardiac muscle was responsible for the failure of contractility. Experiments using cardiac catherization demonstrated no decrease in coronary blood flow, oxygen extraction capacity, or substrate utilization in human subjects with hypertrophy and congestive heart failure. Indeed Dock[4] has pointed out that the coronary blood flow in cardiac hypertrophy without coronary disease is more than adequate to provide oxygen in excess of the requirements. Bing et al.[5] have also reported that the oxygen consumption of patients with failure of valvular origin was normal. In examining the protein content of hypertrophied rat hearts, Sobel and Cohen[6] have demonstrated an increase in the myoglobin and mitochondrial fractions. These apparent increases indicate a further expansion of the oxygen-transporting and oxygen-utilizing systems.

Stress Factor

In a search for the factor or factors responsible for the deficient energy utilization in congestive heart failure, attention has been directed toward the energy-utilizing component of muscle contraction, the actomyosin system.

Early in the development of congestive heart failure an excessive stress is imposed upon the heart, primarily in the form of increased distention. Holland and Klein[7] have suggested that this stress could lead to failure by (1) development of a decrease of excitation-contraction coupling associated with the endoplasmic reticular system; (2) loss of essential electrolytes such as potassium, calcium or sodium; or (3) development of abnormal contractile proteins. Recent findings in the literature suggest that the latter may be the most probable cause. Studies by numerous authors have served to advance our understanding of the mechanism of energy utilization in muscle contraction. Attention has been directed to the three proteins, myosin, actin and tropomyosin, which, together with calcium, function as the primary mediators of muscle contraction and the energy-utilizing system.

Abnormal Actomyosin

Mallov and Robb[8] were the first to report the possibility of the presence of abnormal actomyosin in congestive heart failure. In 1955 Benson[9] reported that dogs in myocardial failure, produced by tricuspid insufficiency and pulmonary stenosis, had a decreased concentration of actomyosin in the heart. In addition, these results suggested that this actomyosin was altered and present in a partially dissociated state. Olson[10] and his group characterized the myosin from similarly produced failing hearts and demonstrated that it had a higher molecular weight (695,000) than myosin from normal hearts (226,000). Extended observations on failing heart myosin by these authors[11,12] demonstrated abnormal patterns in ultra centrifugation and electrophoresis. Small changes in the myosin molecule could have profound changes in its function. Ellenbogen et al.[13] have reported an increase in amide nitrogen of myosin from failing hearts. Such a change could have a gross effect on the functional capacity of myosin. Increase in amide nitrogen implies a decrease in total negative charge, which could affect the hydrogen bonding that would appear to be necessary for the three-stranded helix of myosin proposed by Keilley and Harrington.[14] These authors further suggest that one amino acid, proline, required in the proper sequence, is responsible for the folding of the molecule. If this amino acid were not present in the proper position, an abnormal myosin molecule would result. Since the time when Engelhardt and Lyumbimova[15] reported that myosin possessed adenosinetriphosphatase (ATPase) activity, much concern has been given to this reaction as the intermediate mechanism of energy utilization. While studies on ATPase activity of myosin in heart failure have not produced consistent results, numerous authors have reported reductions in ATPase activity in failing human hearts. This could mean some basic alteration in the myosin molecule or in that restricted site on the myosin molecule concerned with ATPase activity. These and other studies point to the possibility of an abnormal myosin which cannot form a proper complex with actin.

Other authors, reviewed by Bing and Kako,[16] have been concerned with the actomyosin system of human failing hearts. Changes in the myosin molecule were observed to take place during failure which were similar to those reported for the "produced failure" in dogs. In addition, work on glycerol-extracted muscle-fiber bundles from failing human hearts reported that failing human hearts develop less tension and exhibit less contractility than similar fiber bundles prepared from normal hearts. Again it is possible to see how small subtle changes on the myosin molecule could affect gross changes in contractility. According to Weber's hypothesis[17] certain reactive groups suggested as sulfhydryl, phenolic hydroxyl, and alcoholic hydroxyl groups located along the myosin molecule in a specific sequence allow for interaction with a phosphorylated site on the action molecule, with resultant tension development and shortening. It is possible that substitution of an improper amino-acid sequence along this reactive group portion of the myosin chain could affect shortening, but may or may not affect the myosin ATPase activity.

Glycoside-Myosin Complex

It is interesting to note that the digitalis glycosides are of little use in the type of heart failure due to lack of energy production and appear to be effective only in case of deficient energy utilization. Brown, Stafford and Wright[18] have shown that there are three centers in a "cardiac" aglycone molecule which must be present for cardiac activity. These centers are (1) a hydroxyl group at carbon-3; (2) a 14 β-hydroxyl; and (3) an unsaturated lactone ring. Waser,[19] in summarizing his investigations on the interaction between digitalis and contractile proteins, found that a glycoside-myosin complex is formed. This author[20] further found in autoradiographs of muscle bundles, perfused via a small artery with tritiated digitoxin, radioactivity on the outside of the membranes as well as inside the muscle cells. This tends to confirm the dual role widely suggested for the cardiac glycosides. The rationale for use of cardiac glycosides on isolated systems is due to the effect that digitalis has in strengthening the intact failing heart; thus, any action on the pure protein could point to the defect in the failing heart. It is interesting to note the chemical similarity between the active cardiac glycoside centers and the actin-binding sites on the myosin molecule. The formation of a myosin-glycoside complex could be associated with the actin-binding sites on the myosin molecule, thus allowing for the proper interaction with actin.

Compensatory Hyperfunction

When a decompensated heart is subjected to prolonged stress, compensatory hyperfunction (Katz[21]) occurs. Associated with this hyperfunction is an increase in cardiac ribonucleic acid (RNA),[22,23] an increase in myocardial transaminase,[24] and a tremendous increase in the rate of protein synthesis.[25] It is interesting to note that this increased rate of protein synthesis does not occur in hypophysectomized rats.[26] This can be explained by the work of Korner,[27] who suggested that the growth hormone, secreted by the anterior pituitary gland, is required for the combination of messenger RNA and the ribosomal RNA template.

Thus we can see that certain hormones, which appear in excessive quantities in the congestive heart-failure syndrome, can influence other cellular functions than the energy-producing systems. It has been shown that during the initial phase of increased protein synthesis an abnormal contractile protein fraction (actomyosin fraction) can be demonstrated.[6]

Meerson[28] has suggested that cardiac insufficiency may result from a depression of the normal replacement of the contractile elements. This may be analogous to the theory of Comfort,[29] who suggests that every stress imposed upon a structure results in a "wearing out" of that structure. While this may or may not be the case, this stress could affect the protein-synthesis mechanism resulting in improper structures.

In view of the evidence cited for an abnormal contractile protein it would appear that the primary causative factor in myocardial failure is a biochemical defect within the heart which may result in an improper amino-acid incorporation into the contractile proteins.

Comments

At the present time studies are under way in this laboratory to elucidate the amino-acid composition of failing-heart contractile proteins. Using the method of Benson,[9] which we have slightly modified, we have been able to produce congestive heart failure in dogs at much reduced mortality rates. The amino-acid composition of failing-heart myosin, as well as the other contractile proteins, will be reported in separate papers.

The evidence suggested for an abnormal myosin molecule in failing hearts does not exclude the possibility of other abnormal contractile proteins. This possibility is also presently under investigation. The common denominator of most forms of heart failure would still appear to be the inability of the actomyosin system, which forms the myofibrils, to assimilate the energy of the phosphate bond and convert it into kinetic energy of contraction.

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Drive Safely

Cars and bars mean stars and scars. — Defender.

Advice

It is not necessary to take a person's advice to make him feel good — all you have to do is ask it. — Richard Armour

Response of the Myocardium to Drugs

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ALMOST ANY DRUG administered for its systemic action may produce some alterations in myocardial function. Commonly these effects are the result of a compensatory reflex action, not of a direct action on the cardiac muscle. This discussion will be limited to a few of the drugs acting directly on the myocardium.

Cardiac Glycosides

These are myocardial stimulants. They are natural products, those in common clinical use being derived from Digitalis purpura or lanata. The use of glycosides from these particular plants is based more on custom than any actual superiority over glycosides from other natural sources. All cardiac glycosides, regardless of their sources, have a similar pharmacological action.[1]

Chemically, a glycoside consists of an aglycone and a sugar.[2] The aglycone is the active portion of the glycoside. The sugar is attached through a glycosidic linkage to the aglycone; it facilitates tissue penetration of the aglycone and markedly potentiates the latter's cardiotonic action.

Mode of Action

On absorption the cardiac glycosides appear to be distributed throughout the body, at least a portion being bound in the myofibrils.[3] Studies on muscle contraction have established that the myofibril, to contract, requires not only adenosine triphosphate (ATP) but calcium as well.[4] Within limits, the force of cardiac myofibril contraction appears to vary in direct proportion to the level of intracellular calcium.[5] The cardiac glycosides stimulate the rate of flow of calcium into the myofibril.[6] This increase in myofibril calcium may account for the entire cardiotonic action of the glycosides. However, in addition to their effect on calcium, the glycosides tend to favor the outflow of potassium[1,7] and to inhibit sodium-potassium-activated adenosine triphosphatase (Na^+ +

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K^+ − ATPase).[8] The alterations in potassium flux are probably secondary to those of calcium, but the significance of the action on $Na^+ + K^+$ − ATPase is not clear. It may be a manifestation of glycoside toxicity.[9]

Pharmacologic Actions of Cardiac Glycosides

Cardiac Muscle

The cardiac glycosides have no beneficial action on the normal heart muscle; their typical action is seen only on the decompensated heart. The refractory period of cardiac muscle is decreased and the force of ventricular contraction increased. Heart size is reduced toward normal, cardiac output increased, and venous pressure and edema reduced. The over-all effect is an improvement in cardiac efficiency.

Conduction

The refractory period of the AV node and Bundle of His is lengthened. This, along with the general improvement in the circulation, leads to a slowing of the ventricular rate. Slowing occurs despite an actual reduction in the refractory period of the cardiac muscle and an increase in force of ventricular contraction. This action of the glycosides on conduction may be utilized to advantage in auricular flutter and fibrillation. In the former condition, the flutter may be converted to fibrillation, which on withdrawal of the glycoside, may revert to normal rhythm. In addition, in both auricular flutter and fibrillation, the glycosides tend to protect the ventricle from excessive auricular stimulation.

Vagal Action

The cardiac influence of the vagus is increased by the glycosides. In part, this may be due to central vagal stimulation and in part to the improvement in circulation (decreased influence of the Bainbridge Reflex). Also, it is possible that the glycosides reduce the threshold of the SA node to vagal action. These vagal actions contribute to the slowing of the ventricular rate and have a practical application in the control of auricular tachycardia.

Other Action of the Cardiac Glycosides

These are either of minor therapeutic importance or actual manifestations of toxicity.

a. Diuretic Action: The glycosides have some direct diuretic activity and will reduce tubular reabsorption of salt and water. However, this action is not of sufficient magnitude to be of clinical importance. In the presence of cardiac edema, the glycosides produce a marked diuresis, but this is secondary to the general improvement in the circulation.

b. Stimulation of Cardiac Automaticity: This is actually a manifestation of glycoside toxicity. With increased glycoside action, the muscular effects predominate. Myocardial refractory period becomes progressively shorter, and eventually arrhythmias result. Auricular disturbances, premature ventricular contractions, coupling and/or ventricular tachycardia may occur. Although these are manifestations of toxicity, with care this ability of the glycosides to stimulate automaticity may be utilized to stimulate ventricular rhythm in heart block.

TABLE I
Dose and Characteristics of Some Glycoside Preparations

		%	Dose in Mg.				Approximate
Preparation	Route	Absorbed	Initial	Maintenance	Onset of Action	Maximal Effect	Duration of Action
Digitalis USP	PO	10–20	1200	100–200	6 hr.	30 hr.	18–30 days
Digitoxin USP	PO	100	1–1.5	0.05–0.2	2 hr.	12 hr.	20 days
(Crystodigen, etc.)	IV	—	1–1.5	0.05–0.2	30 min.	8 hr.	20 days
Digoxin USP	PO	50	2–4	0.2–0.75	2 hr.	8 hr.	4–7 days
(Lanoxin)	IV	—	0.75–1	0.2–0.75	5 min.	5 hr.	4–7 days
Lanatoside C, NF	PO	10–20	5–10	0.5–2	2 hr.	6–8 hr.	2–3 days
(Cedilanid)	IV	—	1.2–1.6	0.5–1	8 min.	3 hr.	2–3 days
Ouabain USP	PO	unreliable	—	—	—	—	—
	IV	—	0.3–0.5	—	5 min.	90 min.	24 hr.

c. Central Nervous System: This may be stimulated or depressed; the actions are purely manifestations of toxicity. In the early stages neuralgia, paresthesia and malaise predominate; later, anorexia, emesis and visual disturbances are common.

Dosage and Toxicity

The principles of dosage established by Withering in 1785 still apply.[1] "Let it be continued until it either acts on the kidney, the stomach, the pulse or the bowel; let it be stopped at the first appearance of any of these effects." Table 1 lists a few of the common preparations, their usual initial dose and an estimate of their onset and duration of action.

It is of interest that the duration of action of any one preparation appears to be directly related to its ability to be eliminated without metabolic degradation. Digitoxin, with a duration of action of approximately twenty days, is almost completely metabolized, only traces being excreted unchanged.[2] Ouabain, on the other hand, which acts for relatively few hours, appears to be eliminated unchanged in its entirety.[10]

The cardiac glycosides are potent, cumulative drugs. It is difficult for them to be administered without some manifestation of toxicity. Commonly, reduction in dose or drug withdrawal will suffice.[1] However, in cases of severe intoxication where there may be disturbing cardiac arrhythmias, specific treatment may be indicated. The cardiac depressants, quinidine and Pronestyl, are not overly effective in antagonizing the glycoside-induced arrhythmias.[1] Potassium salts have been employed on the assumption that a reciprocal relationship exists between the concentration of myocardial potassium and glycoside toxicity.[1,2] Restoration of normal cardiac rhythm has been reported, but few of the cases have been supported by laboratory data.[1] On the other hand, Gubner and Kallman,[11] in studies on patients with acute poisoning from cardiac glycosides, observed that the intravenous administration of Disodium Versenate, a calcium chelating agent, produced an almost immediate restoration of a normal sinus rhythm.

Sympathomimetic Amines

All sympathomimetic amines will stimulate the myocardium, but due to their marked effects on other systems, only a few find use as myocardial stimulants.[1] Isoprel is the most potent and probably the most useful, but epinephrine, neosynepherine, Wyamine, Aramine and similar agents are probably equally effective. Their action is comparable to that of sympathetic stimulation. The force of ventricular contraction is increased. The myocardial refractory period as well as that of the SA node, the AV node and the Bundle of His is decreased. There is also an increase in cardiac automaticity. The primary disadvantage of these drugs is their fleeting action, a few minutes at the most.

The sympathomimetic amines have their greatest application in the stimulation of ventricular rhythm in heart block or delayed conduction. Also, they may be useful in ventricular asystole. Where chronic stimulation is desired, ephedrine, because of its more prolonged action and ease of administration, is the drug of choice.[1]

Myocardial Depressants

Quinidine and Pronestyl (procaine amide) are the most useful of the cardiac depressants.[1,2] They appear to be identical in their mode of action and are approximately equal in their clinical effectiveness and safety. They are general tissue depressants, acting through their ability to inhibit the efflux of intracellular potassium. They depress the vagus, the SA node and the AV node, and they inhibit conduction through the Bundle of His. Myocardial metabolism is decreased and repolarization is prolonged. In the usual dose, ventricular contractile force is little altered, but is decreased following large doses.

These drugs find their greatest application in those patients where depression of cardiac automaticity is indicated.[1] In the absence of increased automaticity their use may be harmful. They are most useful in the suppression of arrhythmias of auricular origin but are also of value in the control of ventricular arrhythmias. Even under ideal conditions, they are only 60% to 70% effective, although digitalization may perhaps increase the chance of success.

The drugs are relatively slowly but almost completely absorbed on oral administration. Elimination is less efficient and care must be exercised if cumulative toxic effects are to be avoided. Quinidine probably offers the greatest hazard, but procaine amide may be equally hazardous in the presence of congested heart failure or impaired renal function. The most serious effects are cinchonism* and/or vascular collapse.

The cardiac depressants are useful adjuncts in electrical countershock therapy of cardiac arrhythmias. The administration of one of these drugs for a day or two prior to electrotherapy markedly reduces the frequency of immediate relapse, and their continued use tends to prolong the duration of the reestablished rhythm.

Summary

There are a number of drugs which are capable of altering myocardial function but only a few that have a direct cardiac action.

1. The cardiac glycosides are the most useful of the direct acting myocardial stimulants. Unless there is a specific contraindication, i.e., ventricular tachycardia, their use is invariably indicated in cardiac failure.

2. Quinidine and Pronestyl are the most useful cardiac depressants. These drugs have their greatest application where depression of cardiac automaticity is indicated.

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*See Test Your Word Score Page 1333.

JOHN OF MIRFIELD: he composed the BREVIARIUM BARTHOLOMEI, a medical work, probably between 1380 and 1395.

In the BREVIARIUM are some clinical tests of prognostic significance: "If the right eye of a sick man sheds tears, he will die; in the case of a woman, this applies to the left eye. The sole of a patient's right foot should be anointed with lard, which lard is then thrown to any given dog; if the dog eats it without vomiting, the patient will live, but if the dog returns it or makes no attempt to eat it, the patient will die." Mixed up with these mystic and messy investigations is much sound medicine, and even more common sense. For example, if there is any doubt as to whether a person is or is not dead: "apply lightly roasted onion to his nostrils. If he is alive, he will immediately scratch his nose."*

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*Massengill, S. E.: A Sketch of Medicine and Pharmacy, S. E. Massengill Co., Bristol, Tenn.-Va., Ca. 1941, p. 38.

All men are born equal, but it is what they are equal to that counts. — Grit

Glutamic–Oxalacetic Transaminase[*]

Origin
and
Fate

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TRANSAMINATION CAN be defined in general terms as a chemical reaction in which an amino group is transferred from an amino acid to a keto acid without the intermediate appearance of ammonia.

A nonenzymatic reaction was first reported by Needham[1] in 1930 and was described in more detail in 1934 by Herbst and Engel.[2] However, true enzymatic transamination was discovered by Braunstein and Kritsman in 1937.[3] These investigators found an enzyme in pigeon breast muscle which catalyzed the transfer of the amino group from glutamic acid to pyruvic acid. Cammarata and Cohen found 22 additional amino acids that could enter into transaminase reactions.[4] The specific enzyme this paper is concerned with is glutamic-oxalacetic transaminase. The reaction catalyzed by this enzyme is described by the equation:

$$\text{Aspartic acid} + \alpha\text{-keto glutaric acid} \xrightleftharpoons{\text{glutamic-oxalacetic transaminase}} \text{oxalacetic acid} + \text{glutamic acid}$$

Evidence was presented as early as 1945 implicating pyridoxal phosphate as the coenzyme for the above reaction.[5] It is known to be the coenzyme for most transaminase systems.

Much biochemical information is now available concerning glutamic-oxalacetic transaminase. Cohen[6] in 1940 found the optimum temperature was 40°C and the optimum pH was 7.5. The research of Karmen et al.[7] suggested a range for the optimum pH of 7.0 – 8.0. The best preparations of glutamic-oxalacetic transaminase to date[8] indicate (ultracentrifuge) a molecular weight of 110,000. Research carried out on this same preparation suggested that the enzyme may be formed by two polypeptide chains with the same N-terminal amino-acid residue; alanine. Electrophoretic studies have yielded variable results, probably due to the use of progressively purer glutamic-oxalacetic transaminase preparations.[9,10] The most recent study has revealed three anionic and two cationic glutamic-oxalacetic transaminase isozymes.[11] The fractionation work of Cammarata and Cohen, already mentioned,[9] gave a yield of 0.5 gram per 1,000 grams of wet pig-heart tissue. Preliminary research has suggested that the glutamic-oxalacetic transaminase enzyme has two active sites; one for oxalacetate and aspartate and the other for ketoglutarate and glutamate.[12]

The majority of investigators agree there are probably at least two varieties of glutamic-oxalacetic transaminase, one present in high concentration and located in the mitochondria, and the other in the supernatant (soluble) fraction of the cell.[13-16] In addition, one of the above investigators has reported that the nuclear fraction also contains a high amount of glutamic-oxalacetic transaminase activity.[15] Recently an immunochemical difference has been described between the glutamic-oxalacetic transaminase from the mitochondrial and the soluble fractions of the cell.[17] The presence of glutamic-oxalacetic transaminase in the mitochondria may be of significance since this is the site of adenosine triphosphate synthesis.

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Glutamic-oxalacetic transaminase is widely distributed in living organisms. It has been found in blood and many other tissues of animals, in plants and bacteria. Research carried out with tissue homogenates demonstrated that glutamic-oxalacetic transaminase was found in the following tissues of the rat in descending order of activity: heart, skeletal muscle, lung, brain, liver, spleen, prostate and testis.[18] This laboratory has confirmed these results in part; we have found rat heart to contain the highest glutamic-oxalacetic transaminase activity, followed by skeletal muscle and liver in that order.[19] Katsura and Yamamoto have confirmed the low glutamic-oxalacetic transaminase activity of endocrine tissue.[20]

Distribution of Transaminase

It is of interest that there is a further distribution of glutamic-oxalacetic transaminase within the heart. Barbieri was the first to report (1957) that the left ventricular glutamic-oxalacetic transaminase was higher than that of the right ventricle.[21] This finding was confirmed by Redetzki et al. in 1958.[22] Vacek and Sevelova in 1962 noted that experimental hypertension in rabbits (induced by ephedrine or nephrogenic hypertension) resulted in an elevated glutamic-oxalacetic transaminase content in the aorta.[23] Our laboratory has extended this observation to the heart. Blood pressure in rats was elevated by means of desoxycorticosterone acetate or by banding of the abdominal aorta. Such treatment resulted in elevated glutamic-oxalacetic transaminase in the left ventricle of the heart, while right ventricular glutamic-oxalacetic transaminase remained unchanged.[24,25] It is also of interest to note that the glutamic-oxalacetic transaminase content of the left ventricle could be elevated by a 15-minute or by a 60-minute swim.[19]

Serum-Transaminase

The fact that heart muscle contained a high concentration of glutamic-oxalacetic transaminase while very small amounts were present in serum led to the prediction that injuries to the heart could be detected and/or confirmed by a rise in serum-activity-transaminase. This was first demonstrated by LaDue et al. in 1954.[26] Their observations led to a wide variety of experiments designed to relate severity of myocardial infarction to serum-activity-transaminase levels. Since liver and brain also contained relatively large amounts of glutamic-oxalacetic transaminase, disease states involving these organs were also investigated in relation to changes in serum levels of the enzyme.

Skeletal muscle also contains a high concentration of glutamic-oxalacetic transaminase; thus open-chest methods for producing myocardial infarction have the possible added error factor of skeletal muscle injury and release of this glutamic-oxalacetic transaminase into the serum. Due to the possibility of this error, coronary embolization by use of plastic microspheres was utilized. This procedure is relatively atraumatic. Studies using this technique revealed that as little as 5-10% infarction of the heart, involving less than one gram of tissue, resulted in a significant rise in serum-activity-transaminase. Also, the magnitude of serum-activity-transaminase elevation was approximately proportional to the size of the infarct.[27] Brodell et al. have shown that more than 200 grams of cerebral tissue must be involved in an infarct before there will be a significant increase in glutamic-oxalacetic transaminase of the cerebrospinal fluid.[28] However, this laboratory has been unable to demonstrate a significant glutamic-oxalacetic transaminase contribution to the serum due to the surgical procedures attendant on ligation of one of the coronary arteries. Similar results in other laboratories have been obtained by the use of open-chest methods. This adds support to our contention. Coronary artery ligation in dogs caused a 31% decrease in glutamic-oxalacetic transaminase content of the infarcted area of the myocardium and a concomitant 355% increase in serum-activity-transaminase.[29] These investigators also studied glutamic-oxalacetic transaminase and serum-activity-transaminase changes in anoxic rats.[30] Rats were maintained for one hour on 7% oxygen, and then respiratory arrest was induced by further reduction to 3% oxygen. This resulted in a 27% decrease in myocardial glutamic-oxalacetic transaminase, but surprisingly there was no change in serum-activity-transaminase. Since they demonstrated that this was not due to a loss of coenzyme, the authors concluded that a local inactivation of the released glutamic-oxalacetic transaminase must have occurred. No other investigators have repeated this study.

The Degree of Infarction

Other experiments have attempted to relate degree of myocardial infarction to onset, rate of rise and duration of elevation of serum-activity-transaminase. Infarction of the posterior papillary muscle of the left ventricle in dogs caused no change in glutamic-oxalacetic transaminase content of the papillary muscle for the first 40-70 minutes; however the serum-activity-transaminase began to rise approximately 4-6 hours later and reached a maximum of 840 Wroblewski units/ml 18-36 hours post infarction.[31] Some 12-15 hours post infarction the glutamic-oxalacetic transaminase content of the myocardium was decreased to 30-50% of normal. The serum-activity-transaminase usually returns to normal in 4-7 days. It is of interest to note that in myocardial infarction in dogs the type of glutamic-oxalacetic transaminase lost is the soluble fraction.[32] Mitochondrial glutamic-oxalacetic transaminase remains unchanged. Prednisolone administered prior to the infarction will prevent loss of soluble glutamic-oxalacetic transaminase.

Prerequisite of Enzyme Release

These early studies appeared to indicate that necrosis of tissue was a prerequisite to enzyme release, a conclusion reached after rather short-term experiments.[33] The evidence now appears conclusive that cellular permeability changes can occur with a magnitude sufficient to allow glutamic-oxalacetic transaminase to escape into the serum in many conditions. Some investigators have found serum-activity-transaminase levels increased to more than twice the normal levels due to the process of aging.[34] Highman and Altland have shown that exposure to simulated high altitude (32,000 feet) for a short period of time (4 hours) will result in elevated serum-activity-transaminase.[35] This rise has been related to catecholamine release and its effect on cellular permeability rather than to the effects of hypoxia, since epinephrine-in-oil as a pretreatment will exaggerate the response, while Dibenzyline (an adrenergic blocking agent) will diminish the response.

Influence of Exercise

Exercise has also been shown to result in elevated serum-activity-transaminase values. Vacca et al. demonstrated that riding the bicycle ergometer resulted in a rise in serum-activity-transaminase, not due to hemoconcentration caused by sweating.[36] They were of the opinion that cellular permeability was increased by the hypoxic situation existing in the working muscles. The serum-activity-transaminase values continued to rise for at least 2 hours following the exercise but had returned to normal within 24 hours. However, there is other evidence in the literature confirming this view.[37-39] It is of interest to note that physical training (forced walks of 6 hours a day for 17-20 days) enabled rats to walk for 16 hours without any change in serum-activity-transaminase.[39] Untrained animals had large increases in serum-activity-transaminase levels as a result of such exercise. Our laboratory has demonstrated elevated glutamic-oxalacetic transaminase activity in heart, skeletal muscle and liver from exercised rats.[19] The resulting increased gradient of glutamic-oxalacetic transaminase from tissue to serum in these animals would favor increased diffusion of glutamic-oxalacetic transaminase into the serum from the tissues, and perhaps other tissues, and thus might explain, at least in part, the elevated serum-activity-transaminase activity associated with exercise. However, exercise is known to be accompanied by hemoconcentration; thus the elevated serum-activity-transaminase could be merely another reflection of this fact.[40,41]

Extracorporeal Circulation

A final example of a non-necrotic rise in serum-activity-transaminase was found by Walker and Morgan.[42] They observed a rise of up to 100 units/ml after a very short period of extracorporeal circulation. The increase started immediately upon the beginning of cardiopulmonary bypass perfusion and occurred when there was no cardiac or hepatic damage. The authors could offer no explanation.

Clinical Implications

The clinical implications of these observations are clear. There are many conditions in which an elevated serum-activity-transaminase titer does not indicate myocardial damage. A thorough knowledge of the patient's activities of the preceding 24 hours may rule out the possibility of myocardial infarction even though there is an elevated serum-activity-transaminase value. However, the serum-activity-transaminase test has been invaluable as an aid in diagnosis of suspected infarctions. In the most recent studies it was shown that the serum-activity-transaminase level was normal in only one of 379 cases of proven myocardial infarction.[43]

Appearance of Transaminase

The disappearance of glutamic-oxalacetic transaminase from the serum is of considerable clinical importance since "the variability of the serum-activity-transaminase curve in an individual patient parallels the variability of myocardial infarction from patient to patient and underscores the need for serial enzyme determinations obtained as early as possible and at daily intervals thereafter."[43] Also, the rate of disappearance will determine to a large extent the duration of the serum-activity-transaminase elevation.

Dunn et al. in 1958 injected purified glutamic-oxalacetic transaminase intravenously (dogs) and followed its disappearance from the blood.[44] They found ¾ of the injected glutamic-oxalacetic transaminase was gone in 6 hours while the remaining ¼ required up to 72 hours to disappear. Most was lost by diffusion into the interstitial fluid. They found essentially no glutamic-oxalacetic transaminase in the cerebrospinal fluid or urine. A considerable amount of this glutamic-oxalacetic transaminase was excreted via the bile (1,000-2,000 units/24 hours), but it was not correlated with the serum-activity-transaminase levels; thus the investigators tended to disregard this as the physiological route of excretion.

Fleischer and Wakim utilized purified preparations of glutamic-oxalacetic transaminase I (nonmitochondrial) and II (mitochondrial) which they infused intravenously into dogs.[45] They noted that glutamic-oxalacetic transaminase II was cleared from the serum much more rapidly than glutamic-oxalacetic transaminase I.

These investigators reported on this development in much greater detail in 1963.[46] For these experiments they again used glutamic-oxalacetic transaminase I and glutamic-oxalacetic transaminase II. Glutamic-oxalacetic transaminase I, when administered intravenously, moved rapidly into the lymph. It reached maximum activity there in 1-3 hours, and at 30% of the initial serum activity. It required some 4-5 days to be eliminated from the blood to control levels. Urinary excretion was negligible, the total activity appearing in the urine in 48 hours being less than 0.4% of the injected dose. These men demonstrated the decrease in activity in the serum was not due to a loss of coenzyme or to modification (denaturation) of the glutamic-oxalacetic transaminase.

Their studies employing glutamic-oxalacetic transaminase II revealed that it moved into the lymph even more rapidly than glutamic-oxalacetic transaminase I. The maximum activity attained was only 8.6% of the initial serum activity. The urinary excretion in the case of glutamic-oxalacetic transaminase II was also negligible, being less than 0.3% of the administered dose. Only 0.9% of the administered dose of glutamic-oxalacetic transaminase II was present in bile.

Finally, these investigators utilized a substance called "Zymosan." This material causes first an inhibition of, and secondly a proliferation of the reticuloendothelial system. If it is administered 2 hours before the glutamic-oxalacetic transaminase it will delay clearance at first, then later enhance transfer of the enzyme. Their findings are in contrast to those of Henley et al., who reported the enzyme was not sequestered in the reticuloendothelial system.[47]

These are acute experiments, however, and are probably not similar to the conditions existing in myocardial infarction. With infarction there is a gradual progression of dying cells and thus a continued loss of glutamic-oxalacetic transaminase into the serum, which would result in a less rapid clearance of the enzyme from the serum.

Comments

The function of the glutamic-oxalacetic transaminase in myocardial or skeletal muscle remains unknown, but it appears to be closely related to the contractile process.[48] The research carried out in this laboratory indicated that, in general, any condition increasing the work load on a muscular organ results in a elevated glutamic-oxalacetic transaminase content. It is postulated that this may represent an attempt by the organism to convert an increased amount of amino acids to keto acids. The appropriate keto acids could enter the Krebs cycle and result in an elevated production of adenosine triphosphate which would aid the animal in meeting the increased work load. This of course is conjecture and not an established scientific fact.

In summary, it appears that the initial report of LaDue et al.[26] indicating the possible clinical value of the serum-activity-transaminase determination in myocardial infarction has been confirmed and is definitely established as a valuable aid in diagnosis of such cases.

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Man

"What a piece of work is a man! How noble in reason! How infinite in faculty! In form and moving how express and admirable! In action how like an angel! In apprehension how like a god! The beauty of the world! The paragon of animals!" "And yet to me what is this quintessence of dust?" — Hamlet-Shakespeare

Nutrition, Cholesterol

CERTAINLY ONE of the most controversial subjects to arise in any discussion of coronary heart disease is the role of diet in the etiology of the disease — particularly the influence of the amount of fat consumed and, more recently, interest in the composition of the fat in the diet.

Physiology of Lipid Digestion, Absorption and Transport[1]

It is estimated that 40% of the ingested triglycerides are completely hydrolyzed to glycerol and fatty acids with the other 60% undergoing only partial hydrolysis to mono- and diglycerides by the lipases in the intestine in the presence of bile acids. These products of triglyceride hydrolysis together with cholesterol, carotenoids and fat-soluble vitamins are absorbed into the intestinal epithelium. Within the epithelial cells resynthesis of triglycerides occurs, and esters of the sterols and vitamins are formed. This mixture of lipids may become associated with small amounts of protein to form chylomicrons which are discharged into the lacteals, then to the thoracic duct and on to the circulating blood. These chylomicrons, then, are the initial vehicles of lipid transport (mostly triglycerides) and are usually visibly present in plasma only when large amounts of absorbed fat must be transported.

β-lipoproteins

Lipoprotein Lipase

The enzyme lipoprotein lipase, which is liberated or activated by heparin, has as its function the "clearing" of the chylomicron triglyceride, effectively hydrolyzing the triglycerides to free fatty acids and glycerol. This "cleared fat" is taken up to a large extent by the liver where the triglyceride is resynthesized, this time as part of the low density β-lipoproteins, and then released into the blood. These β-lipoproteins probably serve as the transport vehicle of the triglycerides to the adipose tissue. It appears that the cholesterol, cholesterol ester and phospholipid constituents of β-lipoproteins are also synthesized and degraded by the liver.

Alpha Lipoproteins

High density α-lipoproteins are also synthesized by the liver, but their role in fat transport is less well understood. There is a suggestion that they may aid in fabrication of the chylomicron by the intestinal epithelial cells through the donation of a peptide. It may also be possible that newly absorbed cholesterol is carried to the liver by the α-lipoproteins, and, if serum albumin is low, α-lipoproteins may carry some nonesterified fatty acids. The α-lipoproteins are also known to serve as carriers of 17-ketosteroids and α-tocopherol.

Fatty Acids

Fatty acids enter adipose tissue as the triglyceride of β-lipoprotein, but they are

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and Atherosclerosis*

THOMAS A. ANDERSON, Ph.D.**
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mobilized as nonesterified fatty acids. These nonesterified fatty acids are rapidly mobilized by fasting and are also very responsive to the effects of epinephrine.

Susceptibility vs. Lipoprotein Fractions

Attempts have been made to correlate susceptibility to coronary heart disease with elevations in the various lipoprotein fractions. Gofman's Atherogenic Index[2] is an example of a prediction equation designed to measure risk of future clinical coronary disease on the basis of the relative concentration of two serum lipoprotein fractions. Some workers feel that the atherogenic index is no more accurate a predictor than the serum-cholesterol level. There remains little doubt, however, that individuals with a high atherogenic index and/or high serum-cholesterol levels are increased risks for atherosclerotic catastrophes, though not necessarily of the coronary type.[3] It might be noted here that the levels of just about all classes of lipids (phospholipid, triglyceride, cholesterol, lipoproteins) are represented by their champions as the most accurate indicators of risk of coronary heart disease.

The American Medical Association Council on Foods and Nutrition[1] has set a cholesterol level of 280 mg/100 ml. as hypercholesterolemic on the estimate that 95% of the population falls within the range 120-280 mg/100 ml. (average 200 mg/100 ml.). The value for hypertriglyceridemia is given as in excess of 250 mg/100 ml., with 95% of the population falling within the range 30-170 mg/100 ml. (average 100 mg/100 ml.). This is not to say that levels below the limits for hyper-concentration of cholesterol and triglyceride may not be more desirable.

Saturated vs. Unsaturated Fat in the Diet

Regulation of dietary fat intake may have marked effects on serum-cholesterol levels. It was the initial work of Kinsell et al.[4] in 1952 that reported that isocaloric substitution of vegetable oil for animal fat in patients could reduce serum cholesterol and phospholipid concentrations. This fact has been confirmed by a number of other workers.

The choice of animal vs. vegetable or saturated vs. unsaturated to describe the hyper- or hypocholesterolemic effects of a fat is not exactly accurate. For example, butter, which may raise serum cholesterol, contains saturated fatty acids of chain length 6-14 carbon atoms, whereas the saturated fatty acids in lard range from 16-20 carbons and do not appear to be as active in raising serum cholesterol as the shorter-chained fatty acids in butter. Oleic acid, a monounsaturated 18-carbon fatty acid, is not as effective a cholesterol lowering agent as linoleic acid (18:2) or linolenic acid (18:3) or some of the more unsaturated long-chain fatty acids found in fish oil.

Average Diet

The average diet in the United States has a polyunsaturated to saturated fatty acid

(P/S) ratio of about 0.3. In other words, the diet contains approximately three times the amount of saturated fatty acid as unsaturated fatty acids. Wide variations are possible. The polyunsaturated to saturated ratio of safflower oil is nine and for beef tallow the value is approximately 0.04. Diets with polyunsaturated to saturated ratios of one or two are recommended for effective cholesterol lowering.

Mechanism of Reducing Cholesterol

The mechanism by which unsaturated fatty acids reduce serum cholesterol is not completely understood — in fact, opinion on the subject is quite divided.

Influence of Solubility

Wilkens and co-workers[5] theorize that absorption of cholesterol depends upon its solubility in the diet fat. Cholesterol was found to be least soluble in hypocholesterolemic oils and most soluble in those oils affecting the greatest increases in serum cholesterol. The solubility of cholesterol in sunflower seed oil increased with a decrease in the iodine number of the fat, i.e., with hydrogenation or a decrease in amount of unsaturation. This theory may be an oversimplification of a very complex problem, as solubility tests alone are not entirely physiological. However, the findings are of interest and suggest additional study of the phenomenon.

The above theory is contrary to the finding that a polyunsaturated fat, such as trilinolein, compared to tripalmitin, a saturated fat, promotes the absorption of C^{14}-labelled cholesterol and increases its degradation to bile acids.[6] Bile acids represent the major breakdown products of cholesterol. Confirmation of this work by Gordon et al.[7] showed that 0.13 g cholic acid was formed daily by a patient on a butter diet, whereas this figure increased to 0.28 g daily on a corn oil diet.

Still another study by Gerson et al.[7] reported that corn oil lowered the serum cholesterol levels in rats but increased cholesterol biosynthesis and also the tissue content of cholesterol in the heart, aorta, liver, gut and muscle. No change was noted in body cholesterol as a whole, but the increased sterol excretion indicated greater biosynthesis and greater excretion.

Species Difference

There may be a species difference here, since a recent report by Taylor et al.[8] indicated that cholesterol biosynthesis in man may be constant and does not vary with the amount taken in the diet. Theoretically, then, any dietary constituent which would accelerate cholesterol degradation would be of value in lowering serum cholesterol.

The literature is replete with studies of the dietary habits of coconut-eating Polynesians, Eskimos and monks, each study attempting to correlate serum-cholesterol levels with the incidence of cardiovascular problems. Take, for example, the study of Trappist and Benedictine monks.[9] Trappists exist on a frugal vegetarian diet (26% fat), don't heat the rooms in the monastery, don't talk much, and were found to have serum-cholesterol levels lower than those found in Benedictines who were comparatively more affluent, consuming a mixed diet (43% fat). However, no difference in electrocardiographic indication of cardiovascular disease between the two groups was found. This would appear to deter those who equate an increase in blood cholesterol with increased susceptibility to coronary attacks. But no! Keys[10] reexamined the data and concluded that there was sufficient evidence to suggest that Trappists are less prone to coronary heart disease than Benedictines — so the controversy continues.

The Framingham Study[11] has shown that the incidence of coronary heart disease increases with a high serum-cholesterol level; but this same study concluded that there was no significant correlation between the various dietary components and the serum-cholesterol level. These workers suggest the possibility that the diet may have passed some threshold level of cholesterol, fat or some other constituent, beyond which further increment is not associated with an increase in serum cholesterol.

George Mann[12] pretty well sums up the problem in his statement that:

> "The evidence will not support the hypothesis that diet causes coronary heart disease, but the evidence does indicate that a reasonable diet will affect a lowering of levels of total cholesterol in many people and there is reason to suppose that this will reduce the risk of coronary heart disease, even though we cannot prove that supposition."

Mann further suggests that certain patients use the dietary regimens outlined by the American Heart Association[13] and the American Medical Association.[1] He feels that this course of action would be especially appropriate for persons with the high-risk attributes of hypercholesterolemia, hypertension and familial coronary heart disease.

One final note on the relationship of hypercholesterolemia and hypertension and risk of coronary heart disease. Cornfield[14] has presented a very sophisticated, yet convincing, statistical model which indicates a 5-fold difference in risk of coronary heart disease between the upper 5% and lower 5% of the population with respect to serum cholesterol or systolic blood pressure alone, but a 25-fold difference between those who are in the upper 5% of the population with regard to both variables (blood pressure and cholesterol) and those in the lower 5% with respect to both variables.

Effect of Pattern of Food Intake on Lipid Metabolism

The work of Cohn[15] has shown that rats force-fed twice daily the same amount of food they would normally consume in 20-30 small snacks throughout the day evidenced the following: increased body fat, altered thyroid activity, increased urinary nitrogen excretion (decreased utilization of protein) and higher cholesterol levels. He found similar responses in chickens, producing hypercholesterolemia and atherosclerosis by limiting the time of exposure to feed.[16] Since the major calorie load must be metabolized after the evening meal in urban populations, Cohn feels that there might be an advantage in re-education with respect to eating habits. He also suggests that livestock producers should mechanize their feeding practices to produce a leaner product with less animal fat in one of our most important protein sources. It would appear that nutritional surveys should consider how the food is consumed as well as what is eaten.

Smoking and Blood Lipids

There seems to be a pretty definite correlation between smoking and risk of coronary heart disease. The action of nicotine on the cardiovascular system is still the subject of much dispute, particularly as to its effects on the coronary circulation. In a study by Kershbaum and Bellet,[17] cigarette smoking has been shown to cause a rise of 25% in free fatty-acid levels of normal individuals; but in patients with myocardial infarction the elevation was as high as 65%. The rise in free fatty-acid was paralleled by a concomitant increase in urinary catechol amines.

This study also suggested that some impairment of fat tolerance appeared to be caused by cigarette smoking, since post-alimentary lipemia was noted in some patients.

Experiments in dogs showed a hypercholesterolemic response to intravenous nicotine administration, but the extrapolation of this finding to man is questionable.

These effects are apparently the result of epinephrine release which is presumably stimulated by nicotine. Sympathetic ganglionic blockade or adrenalectomy inhibits the effect of smoking on plasma-free fatty-acid levels. So, in addition to the effects of smoking and presumably nicotine on blood pressure and peripheral resistance, we have marked alterations in lipid metabolism.

The above-mentioned study utilized filter cigarettes. It may be that the ultimate test of a good filter would be one that could effectively inhibit the rise in plasma-free fatty-acid levels. You are all familiar, I'm sure, with the slogan LSMFT. I can just visualize, as cigarette advertising becomes scientific, a cigarette company coming out with a slogan which would read LRPNEFAL* — meaning, less rise plasma nonesterified fatty acid levels.

Exercise and Blood-Lipid Levels

Probably the most dramatic reports of the influence of exercise on blood-lipid levels concern the various groups of lumberjacks studied[18] who may consume anywhere from 5000-8000 calories daily with from 200-400 g. of animal fat, yet still maintain serum-cholesterol levels in the normal range.

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*See Test Your Word Score Page 1333.

Gsell and Mayer[19] compared the serum-cholesterol level of the population of a Swiss Alpine village to that of a working class group of similar ethnic origin in the city of Basel. These authors conclude that such dietary factors as the fat content and proportion of saturated and unsaturated fats are probably important in determining the serum-cholesterol level, but "they are less important than the activity factor or they manifest their importance only in physically inactive populations."

Exercise causes a decrease in turbidity of postprandial plasma and an increase in fat utilization, apparently affected by an increase in lipoprotein lipase activity. Another important advantage of adequate exercise is the utilization of a portion of the caloric intake, which is commonly in excess of need. Of course, the advantages of regular exercise extend beyond the effects noted on lipid metabolism; developing a pattern of living which includes some daily physical exertion (in moderation) will help to maintain muscle and vascular tone through the years and also serve as a form of relaxation.

Summary and Conclusions

When one adds the effect of dietary lipids on blood-clotting time and fibrinolysis, as well as the contribution of stress and hypertension, to the risk of coronary heart disease, the list of predisposing factors becomes quite formidable.

What approach to take in the management of the disease? It certainly can't be accomplished through the consideration of diet alone or the management of blood pressure alone. It must rather be a combined approach, just as coronary heart disease itself is influenced by a complex combination of metabolic, mechanical and hormonal factors.

A concerted educational program will be needed to publicize some of the danger signals of approaching coronary heart disease. A highly competitive, middle-aged, slightly obese individual who is a sedentary, heavy smoker with an elevated blood pressure and serum-cholesterol level should have been alerted many years previous to his present condition that he will be a good bet to suffer some sort of cardiovascular accident if he doesn't change his living habits. The American Cancer Society has publicized the seven danger signals of cancer; possibly those with an interest in cardiovascular disease could come up with a similar program establishing danger signals for coronary heart disease.

Preventive medicine seems to be the obvious answer. Counselling on weight control, diet, daily exercise, and certainly on the development of some suitable philosophy of life to enable one to compete adequately without undue stress — all this to be achieved before the first signs of trouble.

I am not suggesting that one set formula can be developed to fit each individual situation: surely the accountant commuting into Los Angeles competing with his fellow commuter for the Sepulveda Boulevard turnoff will react differently to a given amount of fat in the diet than, possibly, a Trappist monk or a South Dakota farmer. However, I, for one, would like to see a more forceful program of education undertaken by those interested in cardiovascular disease to alert people to the possible dangers of improper diet, hypertension, smoking, etc.

Cardiovascular disease is a disease of the affluent society. The objective, as I see it, lies in making suitable adjustments to this environment which we have created for ourselves.

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Side Effects: Side effects are relatively uncommon but among those reported are gastrointestinal irritation, sedation, dizziness, cutaneous manifestations, restlessness and insomnia.

Dosage: For full therapeutic effect – Rx full therapeutic dosage. The recommended initial daily dosages, *given in divided doses,* until diarrhea is controlled, are:

Children:
3 to 6 months–3 mg. (½ tsp.* t.i.d.)
6 to 12 months–4 mg. (½ tsp. q.i.d.)
1 to 2 years–5 mg. (½ tsp. 5 times daily)
2 to 5 years–6 mg. (1 tsp. t.i.d.)
5 to 8 years–8 mg. (1 tsp. q.i.d.)
8 to 12 years–10 mg. (1 tsp. 5 times daily)

Adults: 20 mg. (2 tsp. 5 times daily or 2 tablets 4 times daily) **Based on 4 cc. per teaspoonful.*

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Phenylbutazone has not replaced physiotherapy, x-ray treatment, or local injections of hydrocortisone in the more chronic conditions, but it may advantageously be combined with these measures.

Contraindications

Edema, danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. Because of the increased possibility of toxic reactions, the drug should not be given when the patient is senile, or when other potent chemotherapeutic agents are given concurrently. Large doses of Butazolidin alka are contraindicated in patients with glaucoma.

Precautions

Before prescribing, the physician should obtain a detailed history and perform a complete physical and laboratory examination, including a blood count. The patient should be kept under close supervision and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools. Regular blood counts should be made. The drug should be used with greater care in the elderly.

Warning

If coumarin-type anticoagulants are given simultaneously, the physician should watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea and sulfonamide-type agents and insulin. Patients receiving such concomitant therapy should be carefully observed for this effect.

Adverse Reactions

The most common adverse reactions are nausea, edema and drug rash. The drug may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, generalized allergic reaction, stomatitis, salivary gland enlargement, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia are also possible side effects. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently.

Average Dosage

Initially, give 400 mg. daily (one tablet or capsule q.i.d.), reducing this, if possible, when a favorable therapeutic effect has been obtained. If after one week there has been no response, discontinue the drug. To minimize gastric distress, Butazolidin alka capsules may be the preferred form.

Note: The physician should be fully aware of dosage, precautions, adverse reactions, and contraindications as contained in the complete prescribing information.

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Editorials

The Place of the Basic Sciences in Postgraduate Medical Education

It is generally accepted in undergraduate medical education that a student must be firmly grounded in the basic sciences of anatomy, biochemistry, microbiology and pathology before he can understand the clinical subject matter presented to him later in medical school. After he graduates, he becomes eligible for postgraduate education, which is concerned mainly with new clinical knowledge and techniques of value in everyday practice. In some respects, postgraduate teaching is an extension and amplification of the clinical years of medical school. It assumes that the physician has an adequate command of the prerequisite basic science information necessary for understanding the advanced clinical instruction.

Now it is possible that the organizers of many of the postgraduate programs being offered today overestimate the average physicians' current understanding of the basic sciences. Many doctors readily admit that their knowledge of these subjects has faded and express a need to review them as well as to learn about newer developments in these fundamental fields. Thus, there definitely is a need for basic science education for the practising physician.

However, when it comes to planning or attending medical programs, doctors tend to select those that deal with highly practical clinical topics. This preference is evident in most of the programs of scientific meetings sponsored by medical schools, hospitals and medical societies. Also, a strong clinical orientation is seen in the majority of the more formally organized courses of which the American Medical Association has compiled a list of 1,569 for 1964-1965. For example, less than 40 of these courses can be identified from the titles as being primarily of basic science nature and designed for the general practitioner.

We believe that if a physician has a better understanding of the fundamentals upon which modern diagnosis and therapy are based he will be able to practice a better brand of medicine. This conviction motivated us in the development of the program, "Basic Mechanisms of Heart Disease," portions of which are published in this symposium. The course was designed to provide the practising physician increased knowledge of the fundamental aspects of medical science which apply to the cause, prevention, diagnosis and treatment of heart disease. It was presented

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mainly by the basic science faculty of the University of South Dakota School of Medicine. Subjects included the anatomy and the ultrastructure of the heart, ventricular arrhythmias, the origin and fate of serum transaminases, nutritional factors in the genesis of heart disease, the coronary blood flow, chemistry of heart failure and electrolyte alterations in cardiac disturbances, the response of the myocardium to drugs, the action of normal and abnormal heart valves, and the fundamental nature of heart sounds. In the pathology laboratory the physician was able to personally examine a large number of gross heart specimens and microscopic sections representative of various diseases. The attempt was made throughout the course to provide clinical correlation where possible.

Basic science education is an integral part of continuing education for the practising physician, and it deserves more emphasis in the future. If the physician has a good understanding of the basic biological mechanisms which underlie clinical problems, he will be better able to manage these problems. He will also be in a better position to profit from the many programs of advanced clinical instruction. All of this will give greater assurance that postgraduate education will eventually be translated into improved care for the patient.

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Value of the Two-Year Medical School

BEING AN alumnus of the University of South Dakota and having studied medicine for two years at the same university before transferring to Washington University School of Medicine, where I received my degree of Doctor of Medicine, I have watched with interest the gradual decrease in the number of two-year medical schools in the United States. Ten years ago there were 74 four-year medical schools and six two-year medical schools in this country. In the six two-year medical schools (the University of Mississippi School of Medicine, University of Missouri School of Medicine, Dartmouth Medical School, University of North Dakota School of Medicine, State University of South Dakota School of Medicine, and West Virginia University School of Medicine) 438 students were enrolled. In the 74 four-year schools, 14,079 students were enrolled in the first two years. Thus, approximately 3 per cent of all the students in the first two years of medical school were in the two-year schools. In 1964 the number of two-year medical schools had decreased to three, just half the number that existed ten years ago. The three remaining two-year schools are Dartmouth Medical School, University of North Dakota School of Medicine, and University of South Dakota School of Medicine with a combined enrollment of 271 students. The number of four-year schools in 1964 was 84 with a combined enrollment of 16,948 students in the first two years. Thus, about 1.5 per cent of all medical students were in the two-year medical schools.

The three two-year schools have been in existence longer than fifty years. The two state schools in North Dakota and South Dakota were established in 1905 and 1907, respectively. Dartmouth, however, was established in 1797 and is the third oldest medical school in America, being antedated only by Columbia University College of Physicians & Surgeons in 1769 and by Harvard Medical School in 1783.

Medical education is the most expensive of all types of education, and because the two clinical years are proportionately more expensive than the basic or preclinical years,

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the cost of operation of a four-year medical school is proportionately greater than that of the two-year medical school. It is impractical for some states whose populations are small to attempt to maintain a four-year medical school, not only because of the added expense but also because of the lack of clinical material, which is necessary for the two clinical years.

Whereas it may be theoretically desirable for a student to obtain his entire medical education at the same school, such is not necessarily the case. In fact, there are certain advantages associated with transfer from one institution to another, such as is practiced in European universities. It is possible for the European student to transfer from one institution to another for varying periods of time and to return to the parent institution if he wishes. This permits greater flexibility and presumably provides more mature and broader training.

In addition to the impracticality of maintaining four-year medical schools by certain institutions, such as those in New Hampshire and in North and South Dakota, are such schools undesirable from the standpoint of training a medical student? From personal experience, I am convinced that not only is there no disadvantage but probably a real advantage in attending such a school, because the emphasis is placed exclusively on preclinical teaching; also because of the smallness of the institution, students are more likely to apply themselves intensively and to have closer contact with the faculty.

Unfortunately, the attrition in the first two years of medical school is relatively high. Whether this represents poor selection of candidates for admission to the Freshman class or is due to other reasons, it is difficult to say.[1] The attrition in the first year classes of all medical schools for 1963-1964 was 7.5 per cent; in the second year classes, 3.3 per cent; in the third year classes, 1.2 per cent; and in the fourth year classes, 0.7 per cent. Because of the relatively high attrition at the end of the first two years, the four-year schools usually have vacancies which can be filled by transfers from the two-year schools. Administrators of four-year schools have learned that transfers from schools with which they have had experience have proved satisfactory. Most transfers from two-year medical schools have been to Harvard Medical School. In 1963-1964 "The total number of 26 students transferring from two-year schools to Harvard was more than twice as many as to any other school. Seven schools (Harvard 26, Minnesota 11, Northwestern 9, Marquette 6, Iowa 5, Temple 5, and Wisconsin 5) accounted for about 70 per cent of the students transferring from two-year schools."[1] It is considered difficult to gain admission to Harvard Medical School, and the fact that the largest number of transfers were to this school indicates that students completing two years at the two-year school are well trained and able to maintain their standing with those who have had their first two years at Harvard Medical School. For many years Tulane University School of Medicine accepted transfers from the then existing two-year schools in the South — Mississippi, Alabama, and Florida — and with few exceptions, these transfers did as well as the students who received their first two years of training at Tulane.

Dr. Walter L. Hard,[2] Dean of the School of Medicine at the University of South Dakota, stated that failure of students receiving their first two years of medicine at his school to graduate after transfer to a four-year school is practically nil. "Indeed, in my nineteen years at this school, I know of only two students who failed to complete medical school, and both of these were for psychiatric reasons. Furthermore, I know of only two students who found it necessary to repeat a year, either junior or senior." Of the 650 medical students during Dean Hard's tenure, 75% have graduated in the upper half of their classes. When one compares this record with the experience with the four-year medical schools in which the attrition in the junior and senior years is 1.2% and 0.7% respectively, the two-year schools (at least the State University of South Dakota and presumably the others as well) are doing an excellent job.

There is unquestionably a need for an in-

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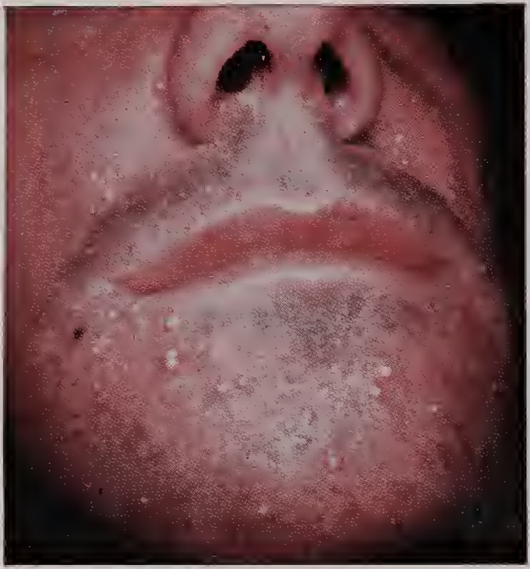

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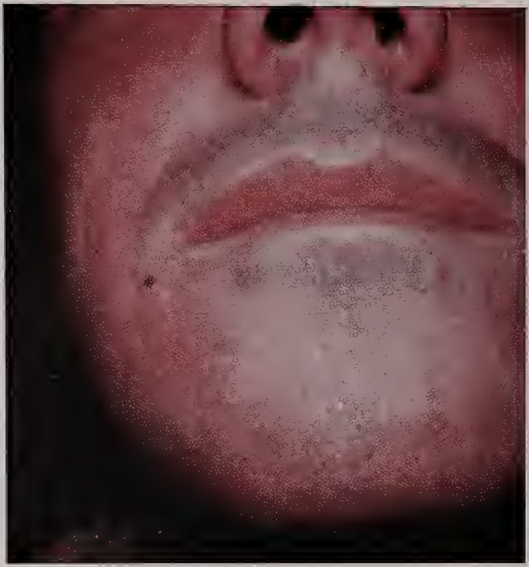

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crease in the number of medical schools to train enough physicians to take care of our rapidly increasing population. Because of state pride the individual states want to have four-year medical schools. This is understandable; but, before embarking on a four-year medical school program, the state should determine whether it is financially able to maintain the expensive third and fourth years, and also whether it is large enough to furnish sufficient clinical material for teaching purposes. The legislatures must be informed of the tremendously increased cost of the four-year school so that if the state is financially able to support it, the legislature will provide the necessary funds to operate the school. Too frequently the costs of a four-year medical school are compared with those of a liberal arts school, and, of course, such a comparison is ridiculous.

An additional advantage of attending a two-year medical school is that generally the cost is much less than it is at a four-year medical school. Obviously, state supported schools have lower tuition than private schools, because they are tax supported. Of the 84 four-year medical schools today, only four have tuition as low as the two state two-year schools. All four are also state schools. In 34 state schools the tuition is higher than in the two two-year state schools. Living expenses are generally less at two-year schools because these schools are in small communities where the medical student can live on a lower budget than if he were attending some of the larger institutions.

A theoretic disadvantage of attending a two-year medical school is that its program might not be correlated with the third and fourth years of the four-year schools. Because, however, most students who have completed the first two years in a two-year school are accepted by a four-year school which has accepted many transfers from that school for many years, more often than not the courses in the two-year school have been planned so that they correlate with those of the four-year school. Therefore, this is not a valid disadvantage. Even if it were, it would be far offset by the advantages of transferring to another institution, a practice greatly encouraged in European universities. At present even among the four-year schools there is an increasing tendency to permit transfer to another institution for one semester on an elective basis. This is highly desirable because it permits the student to obtain a particular phase of training in a branch of medicine in which he is especially interested. In fact, in 1964, 105 students transferred from 50 four-year schools and 47 from other schools, 58 in the third year, and 47 in the second year.

Probably for some time two-year medical schools will continue to exist. Although many medical educators hope that the two-year medical schools can be eliminated, it is my firm conviction that they occupy a real place in modern medical education and that they are serving a distinct purpose. It is far better for sparsely populated states, such as South Dakota and North Dakota, to maintain an efficient two-year medical school than to overextend themselves financially and maintain a second-rate four-year medical school.

Alton Ochsner, M.D. USD'16*
New Orleans, La.

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*Department of Surgery, Ochsner Clinic, New Orleans.

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1. Wiggins, W. S., Secretary, Staff of the Council on Medical Education: Medical Education in the United States. JAMA 190:597, 1964.
2. Hard, Walter, L.: Personal Communication.

Not what men do worthily, but what they do successfully, is what history makes haste to record. — H. W. Beecher.

He knows not when to be silent who knows not when to speak. — Publius Syrus

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The Management of Obesity

NATIONWIDE, MILLIONS of Americans today desperately wish to lose weight. They count calories, go on weird diets, try drugs, join reducing clubs, get advice from radio, TV, and printed articles; many consult their physicians. The results are sometimes spectacular, as witness the announcements by TOPS ("Take Off Pounds Sensibly") of the statistics of their award winners; a loss of "only" one hundred pounds in a year by a woman doesn't come near qualifying for "Queen of Minnesota Tops." (A mere 38-pound loss may be enough for the "King"). But in too many cases the end results are vastly disappointing; either the weight loss is trivial or it is only temporary.

The management of obesity is notoriously a frustrating business; the family physician spends endless time to little avail and concludes that most would-be reducers are inveterate liars; the bathroom scale threatens doctor as well as patient with neurosis. Most obesity clinics and special reducing centers consider their performance above par if in 20 per cent of their patients they obtain a sizeable reduction that is maintained as long as a year.

The worst of it is that it all should be so simple: merely a matter of caloric balance; and tables of calorie values of foods, as well as "foods" with little or no calorie value, are available everywhere. But it is not all that simple. In the first place, it is increasingly apparent that in many cases of obesity, and in the majority of obese children, the abnormality is more on the side of energy expenditure than in the direction of an unusually large food intake. These people exercise too little, they reduce physical activity to a minimum, and when they reluctantly abandon the sedentary posture they move with deliberation; in short, the obese person is apt to be uncommonly successful in energy economy.

It is helpful to realize this fact, but this in itself is no guarantee of success. Getting fat persons to exercise is seldom much easier than to persuade them to stop eating. Besides, it takes more than a few minutes of calisthenics to add up to an appreciable amount of calories.

Ideally, more exercise and less food is the answer; the real target should be to shed fat and to exchange some of the lost fat for more muscle. A pound of weight loss is, on the average, the equivalent of about 3,000 calories of negative balance; a pound of muscle gained corresponds to less than 500 calories of positive balance.

We have discussed these questions in enough detail for patients and most physicians in "Eat Well and Stay Well" (revised edition, Doubleday, pp. 65-99). The needed calorie data on foods are in a table available from "Consultant."*

The purely technical questions are easy; the psychological aspects are much more complicated and their exploration in depth with the individual patient eventually could lead to the psychiatrist's couch. This is not to imply that obese patients are generally neurotic or should be referred to a psychiatrist. In the absence of indications for neurosis other than simply the fact of obesity, we would caution against over-emphasis on this approach.

But, however we rate the emotional factor in the scale of causes of obesity, it is clear that the successful management of obesity demands awareness of the psychological situation. Plenty of patients insist they want to reduce, know that calorie imbalance is the problem, understand the rudiments of calorie values, of food and exercise and still cannot, or at least do not, reduce. Obviously, psychological as well as dietetic problems must be solved.

Fantastic reducing diets, featuring bizarre combinations of food, are periodically promoted and, to the annoyance of serious students of metabolism, they are often at least temporarily successful with some people. In part the explanation is that the re-

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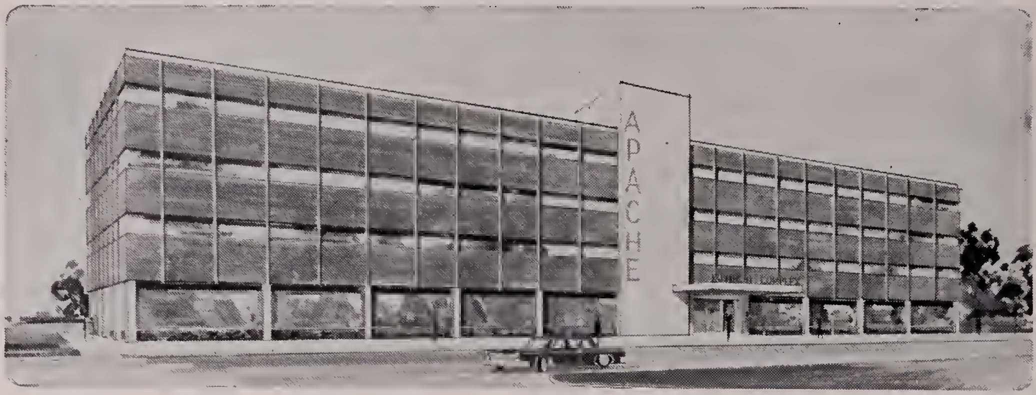
*1500 Spring Garden, Phila., Pa. 19101; 25 copies will be sent gratis to any physician who requests them).



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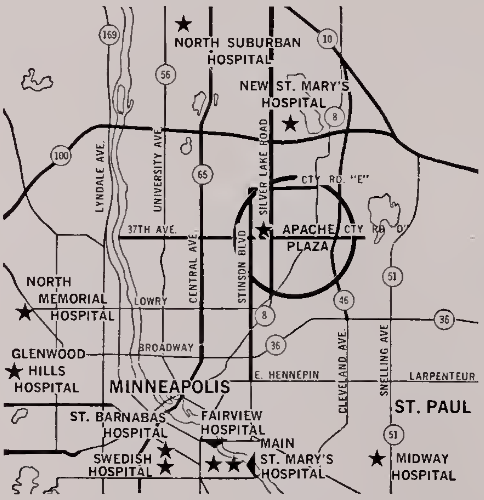
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ducer, caught up in the enthusiasm about a "wonderful new discovery," has new hope, and therefore more will, for real reduction. Perhaps more important is the ego-satisfaction of doing something new, in the latest style, so to speak, and of attracting commiseration for eating such an awful mess. Here is a conversation piece, an attention catcher, that is far more interesting than simply eating less of an ordinary diet. If one must be constantly hungry, some recompense of awe or special sympathy is a great help.

Recently, periods of total starvation have been advocated as an approach to the "hard" cases of extreme obesity.* In the April issue of this journal, Schultz, Werner and Kerlow report on their satisfaction with this method from the experience with 12 patients whose body weights averaged 186 per cent of the so-called "ideal" weight. They ate no food at all for 13 days, lost an average of 23 pounds, reported decreased appetite, and "no serious clinical side effects were observed."

Long ago we observed that total abstinence from food quickly results in loss of appetite; indeed a sense of incipient nausea may develop in a few days, especially if the person engages in physical activity. And the fatter the patients, the better they tolerate such starvation. But even nonobese people get along remarkably well for several weeks with no food if they are sedentary. The professional fasters who attracted attention at the turn of the century often insisted on an unusual sense of well being, even at the end of three or more weeks of fasting; Succi, who was not fat to begin with, had no ill effects from forty days without food.

The professional fasters, besides monetary reward, had much satisfaction from the great attention they received. The obese persons who are given no food at all for a couple of weeks, also enjoy this reward of attention, especially if their heroic feat is undertaken in full view of the hospital staff. And they find they certainly can lose weight.

It is questionable how well the starvation approach will work for the nonhospitalized patients. The constant medical attention is probably unnecessary for their safety but it may be essential for its psychological effect.

Perhaps we should mention drugs that depress the appetite. In selected cases these may be helpful and even advisable for brief periods of time. But they have undesirable and possibly dangerous side-effects and we cannot encourage their general use.

The obesity problem will be with us for a long time to come. It is promoted by an over-abundance of food of high caloric density which we are persuaded to over-eat by all the skills of constant advertising. Often, too, our appetites are increased and our judgments dulled by too much alcohol which by itself adds many calories. And while our calorie intake goes up our output goes down. The wonderful advances of technology not merely free us from back-breaking toil; they make it almost impossible to get a decent amount of calorie-using exercise.

But we trust that we shall not simply give in and accept gluttony and physical indolence as necessary accompaniments to our modern way of life, essential for the food and automobile industries so central in our national economy. We can start with the young and stop the pernicious custom of praising "fine, fat" babies. In the school years we should take a hard look at the high calorie density menus thrust at the youngsters whose only exercise turns out to be some three hours a week in "phy. ed." As civilized adults we can insist that good foods should not be defined as the "richest" and that good cookery does not necessarily mean thick gravies, butter or margarine on everything and dessert "a la mode." We can cultivate contempt for the effort to avoid physical activity. And we can emphasize the fact that in both sexes and at all ages obesity is disgusting as well as a hazard to health.

Ancel Keys**
Minneapolis, Minnesota

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*Bloom, 1959, Metabolism 3:8:214; Duncan, *et al.*, 1962, JAMA 181:309.

**Director Laboratory of Physiological Hygiene, University of Minnesota, Minneapolis.

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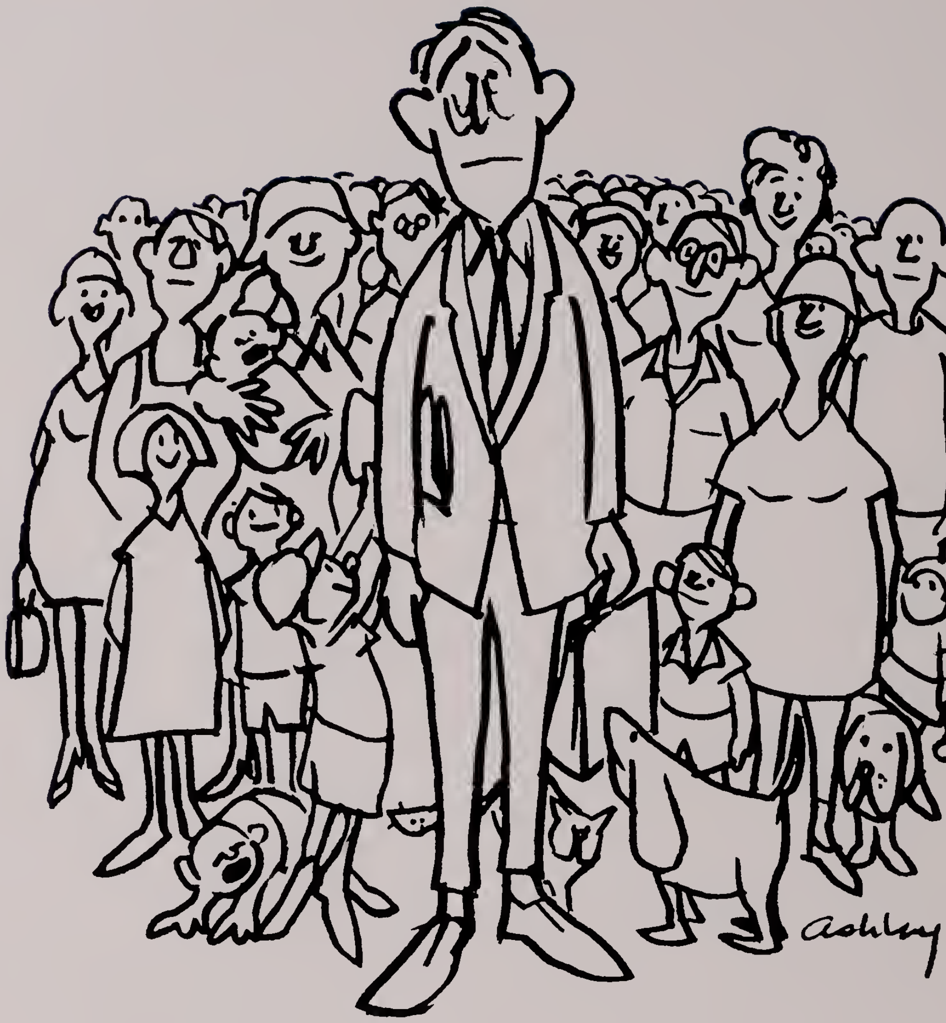

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Cancer of the Stomach

THROUGHOUT THE years the techniques of surgery, anesthesia, and preoperative and postoperative care have been greatly improved. The result has been an encouraging improvement in curability and a decline in operative mortality and morbidity. The results of surgical treatment of carcinoma of the stomach at the Mayo Clinic have been analyzed recently; this study involved 11,817 cases.

At present in our institution, subtotal radical gastrectomy for curative purposes is associated with a mortality of less than 5%; the five-year survival rate obtained with this operation is 50% when the lymph nodes are not involved and 20% when the lymph nodes are involved. The over-all five-year survival rate is about 34%, and we have observed, in the more recent review of our cases, that there is a trend for this rate to improve even more.

In our experience with radical total gastrectomy, the operative mortality has been 14% and the five-year survival rate, about 10%. It should be mentioned that these data apply to adenocarcinomas of the stomach. When the tumors are of the sarcoma type, the mortality with these operations is the same, but the five-year survival rate is considerably higher (about 44%).

At present, of the total number of patients in whom carcinoma of the stomach is diagnosed at the Mayo Clinic, 90% are subjected to laparotomy; the remaining 10% are found to have evidence of widespread metastasis, and surgical exploration is therefore not indicated. Fifty-five per cent are treated by resection; 3 to 4% die at the time of or immediately after operation. Of those who survive the resection, 19% live more than three years after the operation and 15% live more than five years.

The physician should always be alert to detect malignant tumors of the stomach at an early stage. In the treatment of this disease, the histologic classification of the lesion, the mode of spread, and the surgical indications should be borne in mind. Adequate surgical treatment of these tumors offers reasonably satisfactory results with an acceptable operative mortality.

William H. ReMine, M.D.
Rochester, Minnesota

Reference

1. Pack, G. F. and Ariel, I. M.: The Treatment of Gastric Cancer. Minnesota Med 48:747, 1965.

Test Your Word Score

Purkinje — *Johannes Evangelistica P. Bohemian physiologist 1787-1869* (page 1278).
Efflux — *passing away* (page 1290).
Desmosomes — *a small thickening at the middle of an intercellular bridge* (page 1294).
Hyponatremic edema — *sodium salt depletion edema* (page 1299).
Cinchonism — *headache, tinnitis, deafness, cerebral congestion, toxic effects from chincona alkaloids* (page 1308).
LRPNEFAL — *see "Tower of Babel," Minnesota Medicine 45:1259, 1962* (page 1317).
Pragmatism — *a practical approach to problems and affairs — a philosophy provided by C. S. Pierce and William James: thought is to guide action* (page 1335).
Betony — *plant formerly used in medicine, astringent, aromatic, emetic, cathartic* (page 1349).
Lyophilization — *a process of rapid freezing and dehydration under high vacuum* (page 1373).

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Letter to the Editor:

I am sure that all physicians in this state, including the pathologists, have read with interest Dr. S. A. Smith's special article concerning cervical cytology in the February, 1965 issue.

According to this article, 27.4 per cent of Minnesota physicians stated that they did not take routine pap smears. Cost was one of the factors and "the suggestion was often made that the state establish a laboratory to process smears free or at cost." (I question the use of the work "free," unless there are physicians in the state of Minnesota who do not pay any taxes).

If the state were to operate a laboratory, its overhead would probably be no less than the overhead of the pathologists who presently examine the cytology smears in this state. An effective cytology screening program must be closely supervised and controlled by M.D.s specially qualified in cytology.

Doctor Smith's article points out that the great majority of eligible females in the state of Minnesota are being surveyed on a routine basis, with the smears being sent by the local physicians to qualified pathologists. This certainly precludes the need for a state-operated diagnostic cytology laboratory.

Craig W. Freeman, M.D.
President
Minnesota Society of Clinical Pathologists

The Editor's Soliloquy

A Thousand Torches from One Small Flame

The measure and quality of success may require their own definitions for adequate evaluation. That success which is self-directed for personal glory alone is neither permanent nor admirable, as it makes fools falsely esteemed, secretly envied, and servilely flattered by those obsequious ones who love to sit in the shadow of idols. Genuine success is self-effacing. Its vision encompasses all mankind.

In reviewing graduates from the University of South Dakota the roster includes some internationally recognized men: Alton Ochsner (surgeon), Roger D. Reed (penicillin), Harold F. Schuknecht (operation to relieve deafness), Ernest Lawrence (cyclotron designer — instrument to split the atom); the list is too long to be catalogued here; but these few notable figures who have had world-wide impact in the field of medicine amply support the thesis that eminence can emerge from the most humble origins as well as from established-name institutions, and that true success is altruistically, not selfishly motivated and achieved.

To the University of South Dakota, then, may be traced some of the beginnings of a new era — the most super civilization of all time — the age of intellectual pragmatism,* the revolutionary benefits of which, if not foolishly dissipated or misdirected by the politically ambitious, can usher in a neo-millenium.

Carl O. Rice, M.D. U.S.D.'23

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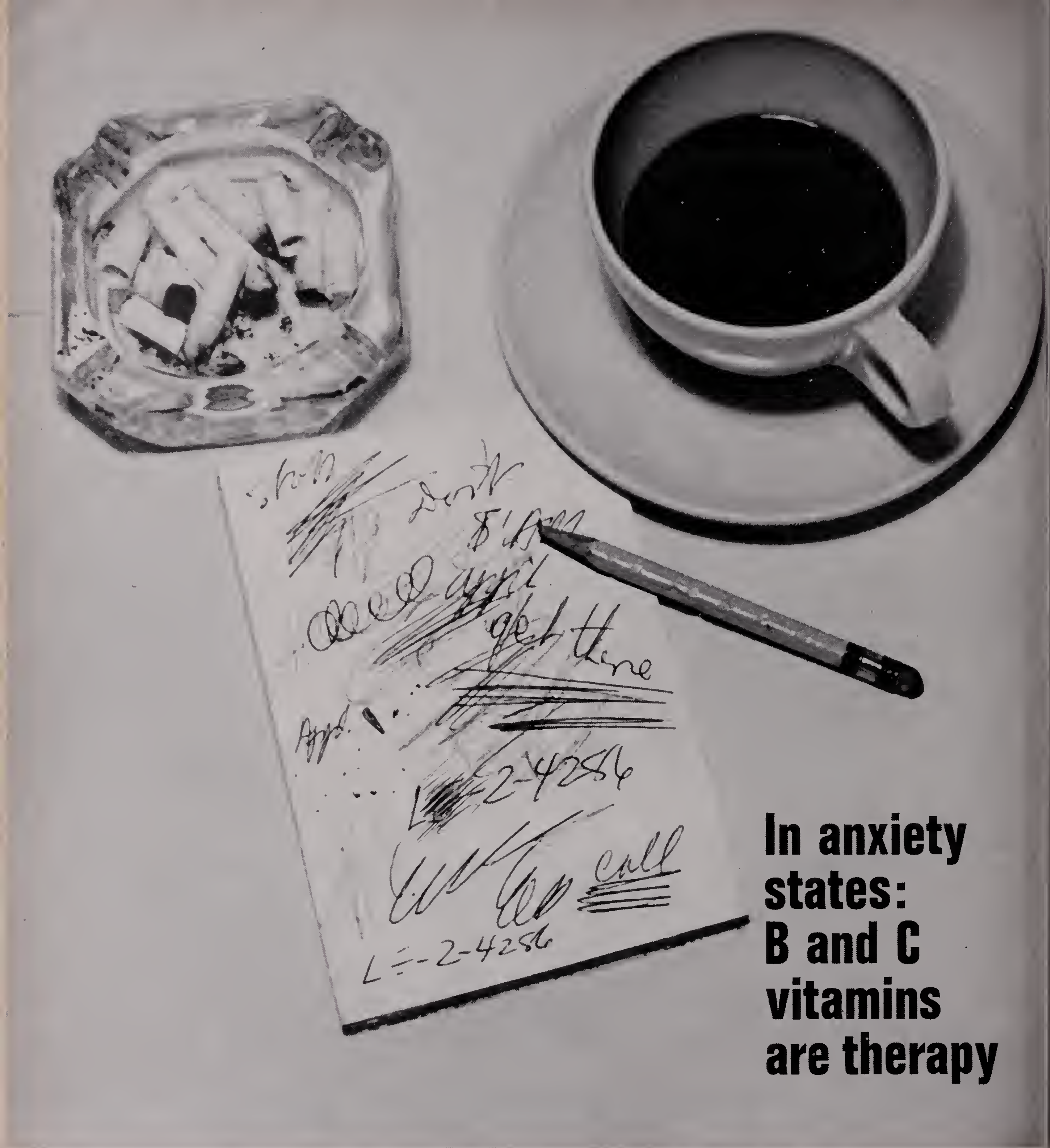
*See Test Your Word Score Page 1333.



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Curbstone Consultation

Acutely Perforated Duodenal Ulcer

QUESTION: I have frequently been involved in discussions with colleagues as to the comparative merits of the management of acutely perforated duodenal ulcer by primary simple closure or emergency gastric resection vs. "conservative" or nonoperative treatment. Is there actually a place for conservative treatment considered alongside the time-honored operative methods for handling these cases? Is one justified in using conservative treatment in the patient who would be classed as a good surgical risk?

ANSWER: Proponents for nonoperative management stress the fact that in most reports conservative management has been reserved for those who refuse surgery or are too ill to survive any operative procedure. Naturally, in such cases the statistical results on behalf of conservative management are going to be poor. When a patient population group similar to those subjected to surgery are managed conservatively, the results are closely parallel.

Since very young and very old tolerate peritonitis poorly, it is probably best to treat these patients by simple closure as soon as they can be adequately prepared for surgery. If one elects to use the conservative method of management, he must thoroughly familiarize himself with the technique, follow the patient very closely, be able to recognize when this method is ineffective and be prepared to abandon it without delay in such cases.

Elimination of Drugs Causing Hepatitis

QUESTION: Would you recommend that drugs which occasionally cause hepatitis be eliminated?

ANSWER: I think that drugs that produce a viral hepatitis-like reaction should be eliminated, but those making cholestasis can be used if patients are watched carefully. Bilirubinuria should be an early sign to indicate withdrawal of therapy.

Fenton Schaffner, M.D.
Mt. Sinai Hospital
New York, New York

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Initial Evaluation of Soft Tissue Hand Injuries

When a penetrating wound or laceration of the hand or fingers is seen, several principles should be considered. The first is, of course, to avoid further damage to the already damaged structures; and the second is to evaluate carefully the extent of injury prior to the patient's going to the operating room and prior to the institution of anesthesia.

The wound about the hand is frequently bleeding quite profusely but no attempt should be made in the emergency room to apply clamps to the bleeding arteries or veins in order to control hemorrhage. There are very few occasions on which hemorrhage cannot be controlled simply by compression with sterile dressings and elevation of the hand. Probing about in a hand wound with poor light may lead to possible disaster, such as the clamping of a nerve. It is important to examine the wound itself for its size, especially in regard to any skin loss. The depth of the wound, however, should not be explored in the Emergency Room.

An x-ray of the injured hand should always be taken to rule out the presence of metallic foreign bodies or fractures.

It should be stated that there are very few tendon injuries which lend themselves to repair outside of the operating room under ideal conditions. Occasionally partial or complete division of extensor tendons in clean wounds can be repaired safely in the emergency room. Flexor tendons or tendon injuries in the fingers should be cared for only under the ideal conditions which exist in the operating room.

Even though the wound is covered, the hand can be examined to evaluate the extent of injuries to tendons and nerves. As much information should be gained as possible prior to the patient's going to the operating room to determine the extent of the injury, although it may be difficult to make a good evaluation of the injury in a young child or in an intoxicated patient.

Injuries to tendons can be detected in a variety of ways. The location of the wound, of course, would give some indication of the possible injuries which exist. The structures which lie in the area of the wound itself should also be considered injured unless one can prove them not to be by evaluation of their function. The status of the flexor tendons can often be quickly determined by merely observing the hand as it lies on the examining table. With lacerations of the tendons, a variation from the normal rest-

Continued

ing position of the hand will be seen. The resting position is one of slight flexion of all the finger joints with increasing amounts of flexion as one proceeds from the index to the little finger.

If one of the fingers is lying flat on the table while the others are flexed in the resting position, it is obvious that there has been some tendon injury.

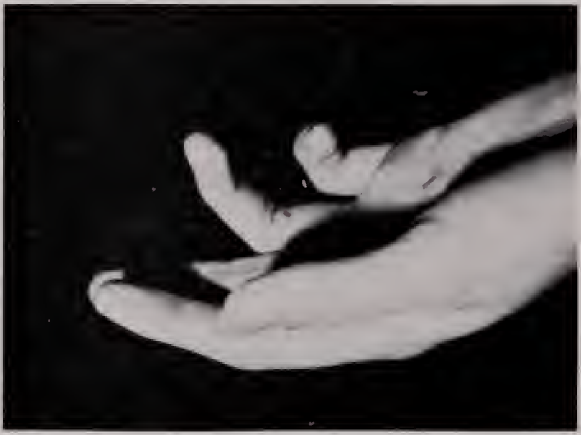

Fig. 1 — Tendon injury obvious from position of fingers.

Specific tests for function of the flexor tendons to the fingers can be carried out. With the middle joint of the finger stabilized, if the distal joint can be actively flexed, the profundus tendon is intact. With the adjoining fingers stabilized in extension, if the patient can actively flex the middle joint of the injured finger, the sublimis tendon is intact. The flexor pollicis longus, which flexes the interphalangeal joint of the thumb, can be tested by stabilizing the MP joint of the thumb.

Injuries to the extensor tendons can sometimes be deceiving unless certain anatomical principles are remembered. An injury to the extensor tendon over the distal joint of the finger will result in the well-known mallet or drop-finger deformity. An injury to the central slip of the extensor tendon proximal to the middle joint of the finger may not be detected immediately if one is not careful to be sure that active extension at each of the finger joints is intact. Extensor tendon injury at the metacarpophalangeal joint may not result in complete loss of finger extension because of the function of the fibers of the dorsal blood. The extensor pollicis

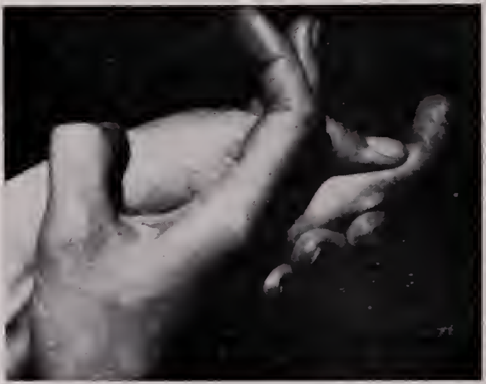

Fig. 2 — Test for profundus function.

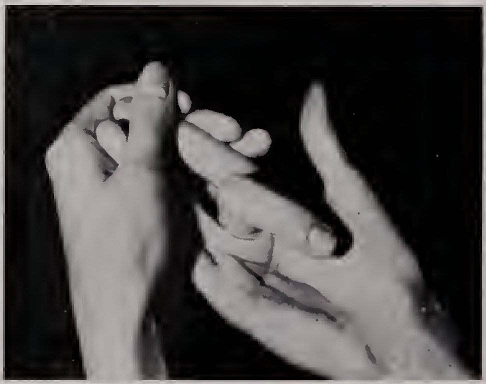

Fig. 3 — Test for sublimis tendon function.

longus tendon must be examined by checking the patient's ability to extend the interphalangeal joint of the thumb.

It should be remembered that partial division of a tendon might not be found by utilizing these methods of examination. This is something which often can only be noted at the time of repair of the wound.

Nerve function should be carefully checked during the initial evaluation of a hand injury. Sensation to light touch should be tested with a wisp of cotton, pain sensation with a pin. Motor function of intrinsic muscles also helps to localize a lesion.

In finger or palmar lacerations the digital nerves are vulnerable. If evidence of severance is noted on examination the nerve ends should be searched for and sutured. Failure to repair these can result in unsatisfactory finger function. If the patient has too much pain or is too excited to respond well it may be necessary to dissect out the nerve to determine if it is injured.

Injury to the radial nerve at the hand or wrist will not result in any loss of motor function. There will be a moderate loss of innervation of the skin over the dorsum of the hand and base of the thumb.

Median nerve function in the hand is generally in jeopardy when there has been a laceration on the volar aspect of the wrist. Whenever one sees a penetrating laceration at wrist level on the flexor surface, the median nerve should be considered lacerated unless it can be proven to be functioning. The chief motor function of the median nerve in the palm is, of course, function of the opponens mechanism of the thumb. Adequate opposition of the thumb is manifested if the patient can actively oppose the pulp of the thumb to the pulp of the long finger. In addition, active function of the abductor pollicis brevis can be checked, for this muscle is almost always (98%) innervated by the median nerve. Skin innervation by the median nerve should be tested; this area involves the volar surfaces of the index and long fingers, and half of the ring finger, along with the radial two thirds of the palm and the flexor surface of the thumb.

Lacerations toward the ulnar side of the wrist or a long laceration involving the entire wrist, should alert one to an ulnar nerve lesion. Motor function of the ulnar nerve can be tested in a variety of ways. One useful test involves evaluating abduction of the long finger, toward both the radial and the ulnar side. This should be done with the palm flat on the examining table to eliminate confusion with the function of the finger

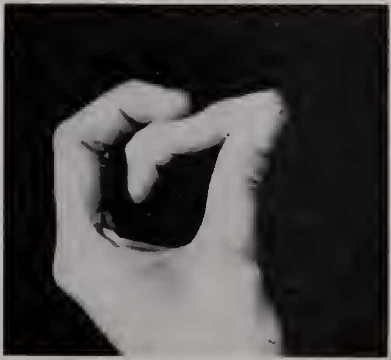

Fig. 4 — Median nerve (opposition).

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extensors and flexors. The adductor pollicis, innervated by the ulnar nerve in 98% of patients, can be tested by Frommen's test. If the adductor pollicis is not functioning the patient uses the long thumb flexor to hold a card or paper between the thumb and the base of the index finger. Adductor pollicis function can also be demonstrated by the patient's ability to place the tip of the thumb against the base of the small finger. The sensory function of the ulnar nerve at the palm involves the ulnar half of the volar surface of the ring finger and the entire volar surface of the small finger, as well as the ulnar one third of the palm.

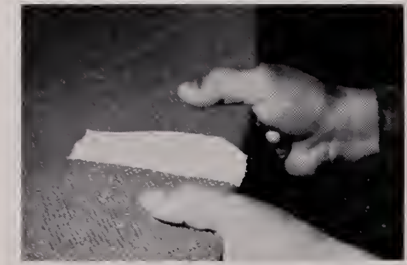

Fig. 5 — Frommen's test. Right thumb shows weakness of adductor.

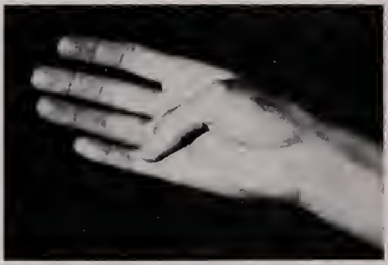

Fig. 6 — Test for adductor pollicis function (ulnar nerve).

Following the evaluation of the extent of the injuries, the patient should then be transferred to the operating room where the remainder of the evaluation is done after anesthesia has been begun. Inspection of the extent of injuries should be made along with and following the irrigation and debridement of the wound.

If the physician in charge of the initial management of the case finds that there is evidence of severe nerve or tendon damage, and he does not feel that he wants to take responsibility for the primary repair of the injured structures, the wound can very nicely be handled by simple cleansing and closure of the skin. Repair of deep structures which are injured can be done at a later date after the laceration has healed.

Joseph M. Tambornino, M.D.
Minneapolis, Minnesota

Overcoming Obstacles

Lincoln is reported to have said: "Some men are like the stump the old farmer had in his field — too hard to uproot, too knotty to split, and too wet and soggy to burn." His neighbors asked him what he did about it.

"Well, now, boys," he answered, "I just plowed around it."

Thomas H. Warner

Blessed is the man who, having nothing to say, abstains from giving us wordy evidence of the fact. — George Eliot

What we do in college is to get over our little-mindedness. — Robert Frost

Tumor Conference

Squamous Cell Carcinoma of the Parotid Gland

Malignant lesions of the parotid gland represent 20 to 35 per cent of all parotid tumors.[1] The following case report is presented because it represents a relatively rare tumor and especially because the approach to therapy stimulated considerable discussion at Miller Hospital Surgical Grand Rounds, and hopefully will interest others.

Case Report

A 58-year-old man was first seen on May 20, 1965, because of a lump in front of the right ear. This was noticed by the patient two and a half to three months previously, and shortly thereafter he noticed difficulty completely closing his right eye and weakness and drooping on the right side of his face. He admitted to some tingling sensation on the right cheek. There was an apparent drooping of the right side of the mouth but no limitation of opening. There was a 2.5 centimeter, nontender, slightly mobile, firm mass anterior to the ear, unattached to the overlying normal appearing skin. Closure of the right eye was possible, but the right facial muscles were generally paretic. Cervical lymphadenopathy was not apparent. The rest of the physical examination was compatible with his age.

X rays of the right parotid area and chest were normal. Laboratory tests were within normal limits.

On May 25, 1965, under general anesthesia, an incision was made over the mass anterior to the right ear, and an incisional biopsy was obtained. Two days later, after a definitive diagnosis of squamous cell carcinoma was confirmed, a radical parotidectomy with sacrifice of the facial nerve, a portion of the right masseter muscle, and a radical neck resection were accomplished. An ellipse of skin surrounding the previous incision with a wide margin was included in the specimen. A free nerve graft, utilizing the greater auricular nerve, was accomplished. The tumor involved the deep lobe of the parotid gland as well as a portion of the right masseter muscle. X-ray therapy was not advised because a good margin of normal tissue was removed surrounding the tumor and lymph node metastasis was not found. The postoperative course was uneventful.

Discussion

Squamous cell carcinoma of the salivary gland is a tumor of high grade histologic and clinical malignancy.[2] It comprised 0.5 per cent of the total and 3 per cent of the malignant parotid tumors in one series.[1] In this same series the three-year recurrence rate in patients with the more highly malignant tumors of the parotid gland was 73 per cent. The five-year survival rate for squamous cell carcinoma of the parotid reported by Arthur G. James in the *Cancer Prognosis Manual* was 19.2 per cent.[3]

Continued

The approach used in this case stimulated considerable discussion, as mentioned previously, since it involved deliberate incision into the tumor, and then delay awaiting permanent sections and examinations by the pathologist. Some felt that with obvious involvement of the facial nerve, resection of the parotid gland and those portions of the facial nerve involved with tumor could be accomplished without definitive pathological confirmation. Another point of discussion centered around the need for awaiting permanent section before planning the operation. Most all agreed a radical neck resection should be part of the therapy, but whether it was done at the same sitting or at a later date was a moot point. It was the feeling of those concerned directly with the care of the patient that better treatment could be accomplished by knowing beforehand the nature of the tumor. The Head and Neck Clinic at Memorial Hospital found that 36 per cent of all patients admitted for treatment of parotid tumors have had one or more previous operations for attempted removal of the growths.[4] It is apparent that at least some of these failures are the result of a poorly planned and hastily conceived operation. Frozen sections of parotid tumors are not always conclusive.[5] Needle biopsy has been advocated in some cases of "malignancies of the parotid clinically diagnosed to substantiate the diagnosis histologically in order to facilitate and plan the proposed operation."[6] Although it has been stated that paralysis had not been noted in the presence of benign tumors,[5] others have stated that infiltration of the nerve is sometimes found with nonmalignant growths,[6] thereby discounting the fact that just because paresis or paralysis is present the lesion is malignant. It seems reasonable that incisional biopsy with subsequent radical removal of the biopsy site, entire tumor, and contents of a radical neck resection offers less chance for spread of tumor than open biopsy at the time of the definitive procedure. In writing about retromandibular parotid tumors, Morfit has stated that the first hint of malignant tumor came only after the mass had been surgically exposed and removal was being attempted.[7] It is probable that many malignant tumors that are not retromandibular in origin are discovered in a similar manner and may account for at least a portion of the failures in therapy.

Summary and Conclusions

A case of squamous cell carcinoma of the parotid is presented, and a method of surgical treatment discussed. A well planned operation after a definitive diagnosis may be helpful in increasing the survival of patients with malignant parotid tumors.

Max E. Harris, M.D.
Lyle A. Tongen, M.D.
St. Paul, Minnesota

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5-7 May be obtained from the author or the reprints.

Neuro-Pediatrics Conference

Cerebral Dysfunction Following Diabetic Acidosis and Coma*

Dr. Robert Bugenstein:**

A four-year-old boy, suffering from diabetes mellitus and mental retardation, was referred to the University of Minnesota Hospitals for further evaluation. He had been followed in the Oxboro Clinic since birth, where he received his routine immunizations. At fourteen months of age he was hospitalized for severe dehydration and coma and discovered to have diabetes mellitus. During his hospital stay he had one or two convulsions which were felt to be due to hypertonic dehydration associated with the diabetic coma. Following discharge he was placed on a 1200-calorie diet and appeared fairly normal except for a paralysis of the left hand and an "off-and-on" twitch in the left eye. Over a period of several months, however, the function in his left hand returned to normal.

At 17 months of age he was able to walk around furniture. At 18 months he had a prolonged grand-mal seizure which did not respond to intravenous glucose but did respond to intramuscular phenobarbital. He was hospitalized, and an electroencephalogram revealed moderate to marked spike-and-wave paroxysmal abnormality focal in the right frontal region. He was placed on Dilantin at this time.

By 20 months of age he was able to walk fairly well and used both hands adequately. At two years of age he was on nine units of regular insulin and twenty-six units of NPH insulin. He was not able to talk but was able to feed himself. When he was 29 months of age, his mother noted that he was having akinetic seizures and was developing hypertrichosis on his arms and legs and some fat atrophy on the upper arms and thighs. Another electroencephalogram was done and interpreted as showing a marked abnormality with continuous spike-wave activities.

At three years of age he was still being maintained on Dilantin, three-a-day and phenobarbital, ½ grain three-a-day; but as the phenobarbital

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*Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatrics conferences are held the first and third Wednesdays of every month from 1:07 to 2:00 p.m. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Charles Branthaver, in Pediatrics, and Dr. Robert Soll, in Adult Neurology.

Held on Wednesday, March 24, 1965, at 1 p.m.

**Referring Physician, Oxboro Clinic, Minneapolis.

Continued

caused hyperactivity, it was discontinued. His growth rate as measured by his height and weight was normal for his age. He was able to say only "ma-ma" and "da-da." He was still being fed by his mother and given a bottle from which to drink milk. His development appeared to be even more grossly retarded than before, and there was no creative pattern in his play. When he was three and a half years old his mother noted that he had a habit of banging his head on furniture or on the floor. He spoke no words but did understand directions.

On his last visit, at age four, he showed increasing hyperactivity and a greater discrepancy between his chronological age and his developmental level which was approximately 15 to 17 months. There was some moderate atopic eczema in the anticubital fossae, the wrist and the backs of his knees. He was started on Desoxyn in an attempt to control his hyperactivity.

Both parents expressed an interest in having the patient seen at the University Hospitals. The mother, who tends to be a very tense individual, came in only periodically for checks with the patient. His diabetes has never been closely controlled, as an attempt has been made to keep him on the side of hyperglycemia in order to avoid any hypoglycemic attacks.

Dr. Sheldon Hess:*

The mother's presenting complaint at the Pediatric Clinic was that she wanted a neurologist and psychologist to look at the patient, explain the extent of brain damage, and also give a prognosis as to what his future development and capabilities might be. She seemed extremely nervous and somewhat hostile.

The patient was the product of a low forceps delivery. Some tremors and a high cry were noted on the first day of life. He was discharged from the hospital on the fourth day in apparently good condition. Eczema was observed at two months of age, which improved with the removal of milk. Polyuria and poor appetite were evident several days before the onset of diabetic coma.

A review of the hospital records at St. Barnabas showed that on admission at 14 months of age he had sunken eyes, was very irritable, and had a weak cry. His blood glucose initially was 1,300; BUN, 37 mgm.% and CO_2-3 meq./ml. The day after admission he had a grand-mal convulsion, and his prognosis was considered very grave; his pupils were dilated and reacted poorly to light. Blood sugars drawn during his hospitalization varied between 72 to 256 milligrams per cent. His electrolytes on the eighth day of admission showed a sodium of 152 meq./ml., and chloride of 113 meq./ml.

Physical examination at the initial University visit showed a non-co-operative, hyperactive child of normal height and weight. There were no significant physical findings and his neurological examination was normal.

Dr. Frank Wright:**

On examination the patient revealed extreme hyperactivity, and no positive neurological signs were noted. His head size of 48 cm. is significantly subnormal, thus correlating with a lack of adequate brain growth and development. Examination of the fundi revealed no vascular changes and no cataracts.

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*Student Physician, University of Minnesota Hospitals.

**Assistant Professor, Pediatrics and Neurology, University of Minnesota Hospitals.

An electroencephalogram showed a moderately to markedly abnormal record, with depression of activity in the right hemisphere, paradoxical slowing in the occipital and temporal regions, paroxysmal irregular polyspikes and slow waves in the right temporal frontal region, and paroxysmal spike activities in the right frontopolar region. The record was compatible with possible atrophy on the right with irritative lesions.

The patient should continue on his anticonvulsant medications indefinitely. In view of his past history the Dilantin should be maintained. Phenobarbital is not indicated, since he had increased hyperactivity on this medication. Equinal has been added to the therapeutic regime in an attempt to calm the patient; however, this has not been satisfactory. Phenothiazid compounds have been tried; but one runs the risk of potentiating a seizure disorder with these drugs.

Dr. Robert ten Bensel:*

It is well known that diabetic acidosis and coma are seen more frequently in younger patients; however, most of the mortality from diabetic acidosis occurs in the elderly patient and is complicated by other disease, particularly arteriosclerotic heart disease. There have been other studies[1] done, showing that the mortality and morbidity of diabetic acidosis is related to the extent of unconsciousness, circulatory collapse, and the degree of hypoglycemia and azotemia, but not to the total CO_2 content. Other authors have commented that in diabetic acidosis the possibility of insulin shock may be one of the major complications leading to cerebral dysfunction. It has been shown that with hypoglycemia there is decreased oxygen consumption by the brain, with three to five per second delta-wave activity on the electroencephalogram.[2] Pathologically, in the brain, there may be cerebral edema, petechiae over the convexity of the cortex nerve-cell alteration, diffuse, focal glial proliferations and areas of demylinization.[3] Gardner[4] states that in hypoglycemia, brain glycogen is decreased, and animal studies have shown that the high centers of the cortex are first affected, followed by the upper brain stem and finally the medulla. Transient hemiplegia and aphasia have been noted to follow diabetic acidosis; however, these usually clear up in a matter of a few days to months.[1] Convulsive disorders, emotional disturbance, and intellectual deterioration have also been noted following diabetic acidosis; but these complications are felt to be exceedingly rare.

Dr. Wright:

The pathological changes in hypernatremia are very similar to those seen in hypoglycemia with cerebral edema: pial hemorrhages which may progress to actual subdural hemorrhages. It is certainly possible that a combination of factors may have been playing a role at the time of this patient's diabetic acidosis and coma. Whatever the cause, he suffered a severe injury and, from the lack of progression since that episode, one would expect little in the way of return in function at this point. His prognosis for any further improvement is very poor.

Dr. Harold Ireton:**

The results of intelligence and related tests indicate severe mental re-

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*Pediatrician and Moderator, University of Minnesota Hospitals.

**Clinical Psychologist, University of Minnesota Hospitals.

Continued

tardation. On the Cattell Infant Intelligence Scale his mental age was 11 months: an I.Q. of 23. On the Vineland Social Maturity Scale his mental-age rating was 16 months (Social Quotient-33). In the testing situation, he was co-operative and quite testable and did not display any serious negative emotional reactions. He reportedly manifests immature behavior in stress situations. The parents' Minnesota Multiphasic Personality Inventories were normal. One other approach to the problem of hyperactivity might consist of helping the parents to handle the stressful situations that arise in the home.

Mrs. Mary Cordingley:*

This mother was a rather quiet, soft-spoken woman, appearing to be very understanding with this extremely hyperactive child. She was somewhat depressed in discussing her family and tended to be self-condemnatory. Her initial attitude was that she was able to take care of this child in the home situation; however, over the past several days, she has become extremely tense and has started condemning herself for inability to handle him. She supervises the daily wild behavior of banging doors, jumping on furniture, playing in the toilet, and dumping drawers and contents. She does not favor placement, because she is particularly aware of the limited nursing staff in state institutions and doubts that this child could get the nursing care he needs.

The father is frank about his inability to accept his child's wild behavior; he was very tense regarding the situation and was willing to discuss placement. At the same time he was understanding and considerate of his wife's feelings and has not pushed the issue with her. He did go to the Hennepin County Welfare Department to initiate arranging for guardianship and placement, but his wife was not included in the initial visit. The Hennepin County Welfare Department is now arranging an interview with him in the near future. Mr. Eddy of the Welfare Department is well acquainted with the facilities which would care for the patient's physical needs adequately. The possibilities at the present time include a trial period at Minneapolis Association of Retarded Children Day Care Center.

The family constellation is made up of three other children: boys aged 21 and 19, and a girl aged 15. Both parents expressed disappointment in the scholastic attainment of their children. The 15-year-old girl is a very shy, withdrawn individual, and this concerns both the parents. She is not doing too well in school, and one canont help but wonder what influence this young retarded child might have on the total adjustment of the family.

In a telephone conversation on March 23rd the mother seemed very distraught and had begun to take the patient's Equinal; since then, she has stopped doing so. Certainly more immediate support is needed for the family. At the present time the parents have planned to affiliate with the Minneapolis Association of Retarded Children to get help in adjusting to the patient's retardation and to provide some interests outside the home.

Dr. Bugenstein:

The mother has probably become more aware of the increasing discrepancy between the patient's chronological and developmental age. She seems to be very protecting of the child and has not been willing to discuss these problems openly with him.

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*Social Worker, University of Minnesota Hospitals.

Dr. Wright:

Possible foster-home placement might be more satisfactory at the present time to allow the family to adjust to a permanent placement situation.

Final Recommendations of the Conference

1. A conference will be held with the parents regarding their son. At this conference, Dr. Wright, Dr. Hess and Mrs. Cordingley will inform the parents of the results of the conference. Hopefully, Mr. Eddy will be able to attend this meeting and attempt to work out possible foster-home arrangements in the immediate future.
2. The parents are encouraged to continue with their state guardianship plans; these should be undertaken promptly, since the institutional waiting lists have a long waiting period.
3. The patient will be discharged from the clinic and returned to the care of Dr. Bugenstein, who will maintain primary medical responsibility for the child.
4. Since a disrupted family situation is present, the possibility of referral to Family and Children's Service should also be considered. This will be discussed at the meeting with the parents.

Robert ten Bensel, M.D.
University of Minnesota Hospitals

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Those Participating in the Conference

Dr. Robert Bugenstein, Referring Physician; Dr. Sheldon Hess, Student Physician; Dr. Frank Wright, Pediatric Neurologist; Dr. Harold Ireton, Clinical Psychologist; Mrs. Mary Cordingley, Social Worker; and Dr. Robert W. ten Bensel, Moderator.

The Penalty of Overweight

Obesity has been shown to be associated with the development of (1) hypertrophy and dilatation of the heart, (2) fatty infiltration of the heart muscle, and (3) coronary atherosclerosis.

— **Cyril M. MacBryde, M.D., Signs & Symptoms Lippincott Co.**

Anglo-Saxon Leechcraft

For broken head, take betony:* bruise it and lay it on the head above; then it unites the wound and healeth. Again, for the same: take garden cress, that which waxeth of itself, and is not sown; put it in the nose, that the smell and the juice may get to the head.

— Joseph Payne, M.D., English Medicine in the Anglo-Saxon Times

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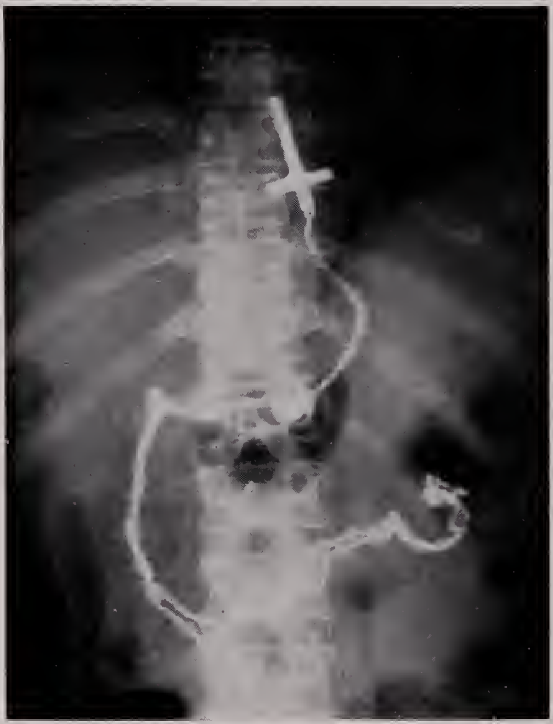
*See Test Your Word Score Page 1333.

WHAT WOULD YOU HAVE DONE?

A 45-year-old white housewife came to the Hennepin County General Hospital with a history of increasing painless jaundice of three weeks' duration. She had been drinking at least a quart of wine daily for the preceding ten years. The physical examination and laboratory studies were compatible with a diagnosis of alcoholic-nutritional hepatic cirrhosis with ascites.

During her hospitalization the jaundice increased and she became confused, lethargic, oliguric and azotemic. Treatment consisted of the usual supportive measures, steroids and diuretics. With this regimen she began to improve.

After two months of hospitalization she developed an acute paranoid psychotic reaction. She put a rosary in her mouth "to keep it from being stolen." She then said that she swallowed it and the following x-ray was obtained. What would you have done? (See page 1369)



Right or Left?

Position or direction is often an important matter in Pliny's, as in magic, ceremonial. It perhaps comes out most frequently in his specification of right or left. An aching tooth should be scarified with the left eye-tooth of a dog; a spider which is placed with oil in the ear should be caught with the left hand; epilepsy may be cured if a virgin touches the sufferer with her right thumb; for ophthalmia of the right eye suspend the right eye of a frog from the patient's neck, and the left eye for the left eye; for lumbago tear off an eagle's feet away from the joint, and use the right foot for the right side and the left for pain in the left side.*

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*Thorndike, Lynn: A History of Magic and Experimental Science, Vol. 1, p. 90. The MacMillan Company, New York, 1923.

Child Psychiatry

Recognition of the Abnormal School Child*

Recent surveys of school populations in various cities reveal that seven to twelve per cent of school age children have emotional problems which deserve professional help.[1] This increasing recognition of the extent of emotional disturbance in children reflects the greater awareness of teachers regarding problem behavior and the addition of trained counselors and special service personnel to school staffs. The marked rise in the public mental hospital population of the ten to fourteen-year age group in recent years as compared to a decrease in the adult hospital population also indicates the greater awareness of children's problems.

Children's abnormal behavior, if not indicative of a physical problem, is often a symptom of underlying emotional conflict. The behavioral signs usually appear early in a minor form and, if unheeded, progress to more noticeable or more pervasive symptoms, all of which represent the child's "cry for help."

In evaluating any child's behavior or emotional problems, we should look beyond the presenting symptoms to the total child and his broad adjustment. Often this includes a consideration of his family and how they are functioning in their individual inter-relationships and also as a group. The physician who knows and treats the whole family and who has been in the home repeatedly, has a most useful insight to contribute which may not otherwise be available.

Infantile Habit Patterns

Emotional and behavioral problems in children often go unnoticed during the first five years while the child is primarily at home; but when the child enters school, he is for the first time seen in comparison to his peer group by a school staff who have a neutral outlook. At this point behavior traits may take on new meaning.

Children begin school at about age five when they are emotionally through the early developmental years and are ready to direct their energy primarily toward intellectual learning and academic competition. Some children, however, still retain infantile habit patterns which suggest prolonged emotional immaturity. These include thumb-sucking, rocking back and forth, extreme dependency and shyness, toilet-training problems, inability to tolerate even the mild competition of the group, or inability to stay in their seat in class. These are children who did not receive sufficient gratification of infantile emotional needs, or whose needs were stronger than usual and not as easily satisfied. Their infantile patterns may interfere with their ability to adjust to the classroom situation and to learn in school. If such children are otherwise happy, relaxed, and socially well adjusted outside the school setting, their persisting habits may not be of specific concern and will disappear with maturation. Angry, punitive parental attention does not help the child to grow out of these habits.

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*Presented May 18, 1965, Minnesota State Medical Association Annual Meeting in Minneapolis, Minnesota.

Continued

If these infantile habit patterns persist, they suggest deeper emotional problems and should be further evaluated.

Hyperactive Behavior

Hyperactive children quickly receive attention from the school. These children present a picture of impulsive, restless behavior with a short attention span, poor concentration ability and impaired visual-motor coordination. They are easily distracted. They frequently disrupt the class and upset the teacher by their continual talking and random physical activity. The hyperactive behavior syndrome is seen more in boys and often is first noticed when the youngster is seven or eight years old. If hostile-aggressive or destructive behavior is also present, the child may be so difficult that he cannot be tolerated in the classroom situation. Hyperactive children usually present more of a problem in school where activity and the large class group overstimulate them beyond the tolerance of their inner controls. In quiet surroundings or in a one-to-one relationship they are not so upset, and they can play and learn more satisfactorily. They often receive help sooner than the quiet, introverted child who may be much more disturbed basically but does not attract so much notice.

Hyperactive behavior is not infrequently seen in children with demonstrable neurological findings and a specific history of a brain-damaging illness; then a causal relationship is likely. Retarded neurophysiologic maturation, which can be inherent or a result of negative emotional experiences in infancy, may produce the picture of the hyperactive syndrome with diffuse undefined cerebral dysfunction. As some abnormality in the electroencephalogram is found in approximately one third of all children, this test itself is not diagnostic for brain damage. Moreover, the diagnosis of brain damage does not invariably mean the problem is irreversible and untreatable. The hyperactive behavior syndrome has often been erroneously equated with organic brain damage. Such false equation may minimize attention to emotional problems which can cause identical behavior symptoms.

Identical hyperactive behavior is observed in children who have suffered gross deprivation of maternal affection in infancy. This, in the past, was particularly observed in children reared in orphanages and other such large institutions with inadequate adult staffing. This degree of severe emotional neglect is seen in some families where it produces the hyperactive pattern with poorly internalized impulse control and a persistent random seeking for unfulfilled emotional gratification. The hyperactive pattern may also result when a child is unwanted or a mother does not have the emotional capacity to adequately provide affectional nourishment and support to the infant. Similar behavior is shown by children whose parents unconsciously expect them to be overactive, uncontrolled and difficult to handle because of the parents' own early experiences. In such instances a careful evaluation of the inter-relationship between the child and both his parents is essential for adequate diagnostic understanding.

Whatever the cause, hyperactive behavior patterns produce frustration in these children because of their inability to conform or achieve up to their potential. Superimposed emotional conflict results, adding to the total problem.

The hyperactive behavior syndrome is one of few conditions in child psychiatry where one occasionally obtains a sudden dramatic response to medication. Moderately strong tranquilizers, such as Mellaril® and Librium,® are often effective. Sedatives, particularly phenobarbital, will quite often increase activity, while stimulants such as dextroamphetamine or Ritalin paradoxically have a calming effect. Unfortunately, the response is often not a lasting one and in a period of two to six months, the child may again present the same problems. Anticonvulsant medication may be effective if the child has specific organic cerebral disease.

Hyperactive behavior often disappears as the child enters adolescence. This emphasizes the importance of these children having help with the frustrating consequences of their problem so that they may enter adolescence with sufficient emotional health and optimism to make the best use of subsequent experiences.

Related to the hyperactive child we see children who are not so much hyperactive as constantly restless, uneasy and impatient, and who may be described by the parents as tense, high strung, jittery or nervous. These children may have tension-relieving habits which seem to be most annoying to adults, especially parents. Such habits include tics of the face, head, eyes, and throat. Sometimes open masturbation is observed in these children or they display rhythmic, tension-relieving behavior which is masturbatory-equivalent. These children are often found to be reacting to an excess of parental control, criticism, reminding and nagging. They are constantly in movement as if to please their parents by the amount of activity rather than the quality of its direction as well as to relieve their own tension. These children are frequently resented by parents or have proven to be a disappointment to them. The parents' attitudes are conveyed to the children by excessive negative criticism.

Neurotic Learning Problems

Many children have learning problems which arise from neurotic inhibition or suppression of curiosity. Such problems are often serious as far as their influence on the child's future academic life and his total productive capacity as an adult are concerned. Specific reading disability is such a problem, in which the youngster fails to acquire reading skills. If this is not detected and evaluated early so that remedial help can be given, the child soon finds himself hopelessly behind the rest of his class. So much of education is dependent on reading that before long there is little reward for him in any area in school. Specific reading disability may be related to an intense suppression of visual curiosity in the preschool period because of repeated admonitions from the parents not to be curious, investigate, or "get into things" as children normally do. Some children witness scenes so unpleasant that they prefer not to continue looking, and this may interfere with reading proficiency in school.

There also can be more general suppression of learning curiosity. This may be reflected by apathy toward school generally, even in the presence of superior intelligence. Such learning problems contribute strongly to a school drop-out problem. When such a youngster gravitates toward other scholastically unmotivated adolescents, this problem may contribute to delinquency.

Nonlearning may be the child's passive-aggressive way of defying his

Continued

parents' insistent demands that he study and learn so that they may be pleased with their own parental accomplishment. The strong positive relationship between parents and child which would motivate him to want to do well in school in order to please his parents is absent. The love and the positive feelings are lacking and the child primarily senses the impatient demand from his parents, which he is not willing to acceed to; hence he resists learning as a way of withholding affection from them.

A child may be aware of his parents' negative attitude about his school, teachers or about education. For the child exposed to these attitudes to be obedient and compliant, he must adopt the same negative attitudes for himself. Open or covert defiance of the school staff and academic progress may result. In such a situation, the attitudes of the parents need to be exposed and modified before the child can be expected to change. In such families the parents often subtly enjoy the child's defiance of school and the disturbance he creates there and, although they make conscious efforts to discipline him, the child is more responsive to their unconscious expectations of him. It becomes additionally confusing to the youngster when he finds his parents punish him for the very behavior which their underlying attitudes encourage him to display.

Another category of nonlearning includes the child who has been so completely overwhelmed by parental overindulgence and overprotection that he has not had an opportunity to learn to think and act independently. Children gradually acquire the ability to think for themselves, to use their initiative, to learn from experience and to take responsibility. If parents lose sight of the fact that their child is constantly maturing and do not transfer responsibility to him gradually, the child may fall into a pattern of passive withdrawal and avoidance of any initiative on his own behalf. This is a comfortable pattern for him since, by making no decisions, he does not have to take the responsibility for his own decisions. As these youngsters enter adolescence, their passive dependency may be so great as to preclude any further emotional growth or academic progress.

Neurotic Children

Anxious, neurotic children comprise another large group of children with emotional problems. Attacks of acute anxiety may occur in children at any age but are seen more frequently between ten and fifteen years of age.[2] The child who suffers acute anxiety episodes usually has a history of previous anxiety which may have been less pronounced and went unnoticed. The anxiety may reach hysterical proportions; an acute episode can be precipitated by almost any emotionally traumatizing experience. A death, illness, or accident in the family or even in the neighborhood may serve to bring underlying anxiety to the surface. Some anxiety arises out of the child's conflict about his own hostile destructive wishes toward those on whom he is dependent. Such a child may lose his appetite, experience nausea, vomiting, stomachaches, and headaches; he may have serious sleep disturbances and nightmares. His anxiety is often related to body function and expressed as a fear that his heart will stop, that he can't swallow, or that he will stop breathing. Death is often involved in his fears, as is being killed or kidnapped.

More commonly we see the child without acute episodes of anxiety but who shows persistent neurotic anxiety and is very fearful about certain situations. He is often frightened at night and resists going to bed. Some restriction of play activity is common because of fear. He doesn't like to go away from home to play. He is too anxious to spend a night at a friend's home or even with a relative and may become quite upset if the parents leave home and a babysitter comes. He may often be frightened by storms or the dark or have peculiar food fears or ritualistic anxieties about clothing. Obsessive-compulsive habit patterns are commonly seen in this group and represent efforts to bargain with the conscience in order to control inner fears.

Some anxiety, sleep disturbance, and phobic concern is normally observed at age six or seven, before the child enters the latency period of his emotional development. However, persistence of such symptoms to any degree becomes significant, particularly if the child's whole personality and energy are invested in the neurotic conflict. If the anxiety is considerable, it will affect the youngster's attitude at home, his adjustment to his siblings, his relationships with his playmates, and his performance in school. Allowing this neurotic anxiety to persist for any length of time permits it to become more deeply entrenched in the child's personality structure.

Tranquilizer medication is of relatively little value, although it may offer brief support and reassurance. In neurotic children anxiety is usually so pervasive that medication does not offer substantial relief. They do respond well to psychotherapy, however.

One specific neurotic problem which we see only in school children is "school phobia." However, it does not represent a phobia of school itself but an anxiety about separation from the parent.[3] In this problem a dependent child is unable to separate himself from a (often unconsciously) clinging parent each morning in order to go to school. The involved parent, usually the mother, does not really want the child to leave and communicates this to the child in various subtle ways. On the surface the parent makes obvious efforts to send the child to school and even punishes him harshly for not going as demanded. The problem first creates concern at about eight or nine years of age, although in retrospect one can see the beginning of the separation anxiety in kindergarten and the first grade. The affected child is often an only child in the family or the youngest, a timid, shy child who is passive and dependent on the parent. For the first year or two in school, the child is able to suppress his fear of leaving the protective home situation, but eventually, usually following an illness or a vacation which allows him to stay at home for a few weeks in a situation of happy dependency, the child becomes extremely reluctant to return to school. Characteristically, once he gets to school for the day and the parent leaves the scene, the youngster relaxes and is relatively comfortable. The next morning he presents the same anxiety, however. The intense fear is most noticed at the beginning of the week and immediately after a school vacation. Treatment of this problem involves concurrent treatment of the parents. These parents often reflect an emptiness in their own life which gives rise to their deep reluctance to let their child leave them to go to school and thus to grow up and away from them. Occasionally we see school-phobia reactions persisting into early adolescence. When this occurs it is indicative of a deeper disturbance. A severe and often incapacitating hostile-dependent relationship may then exist between the adolescent

Continued

and involved parent. Some older children with school phobia become extremely withdrawn and progress to a schizophrenic illness in adolescence.

Depression

More depression exists in children than is often recognized. Depression may be disguised by a multiplicity of psychosomatic complaints or by a withdrawal into an apathetic adjustment which goes unnoticed. Such children feel empty, discouraged, and often entertain thoughts of dying; occasionally these are acted out suicidally in what appear to be accidental childhood deaths. In early adolescence the depression is less masked and suicide is one of the more common causes of death. There is an element of strong hostility in adolescents who attempt suicide. The anger is usually aimed at the parents, or it may be diffusely directed against authority in general. These youngsters are literally angry enough to kill, and whether they kill themself or the hated parent may be a close decision. Occasionally adolescents express their suicidal thinking or other unhappy preoccupations in themes they write at school. Teachers have become quite perceptive in picking up the significance of the content in such writings. Any real suicide threat or attempt by a child or adolescent should not be ignored, although some of the threats are impulsive and do not indicate that the teenager is self-destructive. Hospitalization, however, is usually not indicated for these youngsters. When confined they lose what little freedom they had and their resentment is mobilized against the very adult authority they are fighting. This provokes more anger and also gives them a new focus for their anger rather than an opportunity to work through their original hostility and conflict.

Delinquency

Delinquent behavior in the preadolescent and in the adolescent is another broad area which the physician should recognize as often being an expression of underlying feelings. In a child from a socially deprived home in which he is presented constantly with delinquent patterns or a delinquent neighborhood environment, antisocial acting-out behavior may occur as a rather natural consequence of external influences. Such a child may present a social problem in the community and still not have any specific psychiatric or personality problem himself. However, predelinquent or delinquent behavior in a child from a better socioeconomic background and a cohesive family should alert one that the child may be trying to express something by his behavior, such as his unhappiness or discomfort under pressures in his situation. His delinquency may be a covert attack against his parents and what they stand for. Sometimes it is a poorly concealed effort to get himself removed from his home where he feels the demands are more than he can tolerate. True psychopathic or sociopathic character disorders with absence of conscience or super-ego development are very infrequent in adolescents, although the angry, indifferent or defiant facade behind which many delinquents hide their vulnerable, real feelings may often resemble the character structure of the psychopath.

Psychotic Disturbances

Withdrawal into fantasy is quite common in children and adolescents, even to an extent that would be considered psychotic in adults. A frank psychosis is infrequent in childhood but may occur. Infantile autism describes a very early psychotic disturbance in which a young child exists in his own world of fantasy and relates to people as if they were inanimate objects. An acute psychotic illness is rare in childhood and is suggestive of a toxic or organic etiology. Childhood schizophrenia may develop as a gradual, progressive process. With the onset of adolescence a weakening of ego strength occurs concurrent with the internal and social pressures accompanying puberty. If the ego is not strong enough to contain the instinctual drives and impulses, decompensation into a schizophrenic illness may take place. This happens particularly in the previously shy, withdrawn, oversensitive youngster. The adolescent who has used obsessive-compulsive defense mechanisms extensively may also experience a schizophrenic psychosis as his defenses break down. The diagnosis of schizophrenia in adolescence is more difficult to establish than in adults. Adolescents are frequently diagnosed incorrectly as schizophrenic because of behavior which, although at times associated with schizophrenia, may also be characteristically adolescent.[4]

School's Role

The school setting offers an excellent observation and detection opportunity for the early recognition of children with emotional disturbances and behavior problems. Schools at present, however, can do little more than observe and occasionally offer some diagnostic screening by psychological tests. Such test results, including measurement of the I.Q. and academic achievement, are usually available to the physician and can prove most helpful in his evaluation of a child's emotional status. When school personnel encounter abnormal behavior in children, they often need the physician's help in effecting an adequate referral to the child psychiatrist or other appropriate community resource. Effective evaluation and treatment of the child with emotional conflict often involve treatment of one or both parents.

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Hope is the gay, skylarking pajamas we wear over yesterday's bruises.
— De Casseres

Derivatively Speaking

furuncle: from Latin *furunculus,* a petty thief.

A man's reach should exceed his grasp — Robert Browning

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Athletic Injuries

Evaluation and Immediate Treatment of Soft Tissue Knee Injuries Sustained in Athletics*

The knee is probably the most vulnerable of all the joints to athletic injury. Its anatomy is such that stability is present only because of the ligamentous structures and quadriceps mechanism. It is a flat hinge joint with a sliding component as the tibia flexes and extends on the femur. It lacks the ball-and-socket construction of the hip and the mortise of the ankle from which to gain its stability. Furthermore, it is vulnerable because of the length of the lever arms of the bones which articulate to form the knee joint.

Contusion, torsion, and angulatory strain are the forces which result in injury to the knee joint. Pain and swelling (effusion) are undoubtedly the most frequent symptom and sign of knee-joint trouble; and the usual etiology is traumatic synovitis secondary to contusion, twisting, or forced angulation. Once again, it is the team physician seeing the player immediately after injury who has the best opportunity to make an accurate diagnosis of the injury and of its severity.

Diagnosis

The reaction of the athlete to his injury immediately after it has happened is often an elucidating sign as to how seriously he has been hurt. If he has full range of motion of the knee and can bear weight without persistent pain, chances are that his recovery will be rapid without residual disability. On the other hand, if the knee is locked or unstable, or if the pain is "unbearable," that athlete may be in for a long period of rehabilitation, including possible surgery, with a high probability of permanent disability.

Physical examination of the knee at the scene of the injury should include the testing of the lateral stability, both with the knee fully extended and with the knee flexed 30 degrees. Instability with the knee in full extension indicates rupture of at least one of the cruciate ligaments as well as the collateral ligament involved; instability only at 30 degrees indicates rupture of the collateral ligament in question. The anterior "drawer sign" is a more specific test for the anterior cruciate, and the posterior "drawer sign" for the posterior cruciate ligament. The test consists merely of either pulling the tibia anteriorly on the femur, or pushing it posteriorly; excessive motion means ruptured ligament.

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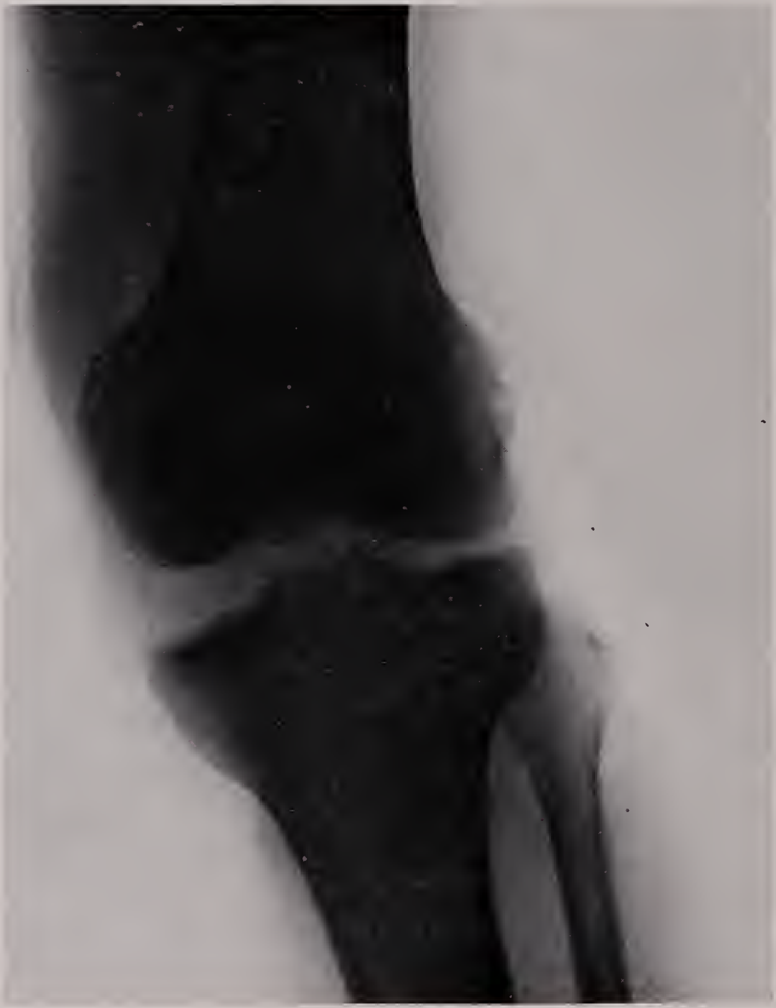
*See Minnesota Med 48:1173 for first in this series. Sponsored by Minnesota Committee on Trauma of the American College of Surgeons.

Continued

A locked knee suggests strongly the possibility of a torn meniscus. The medial meniscus is much more apt to be injured than the lateral because of its configuration and because of its intimate attachment to the medial collateral ligament. With a sprain of the medial collateral ligament, the medial meniscus is also often torn.

X-rays should be taken in three views: AP, AP tunnel view, and lateral. Stress films are indicated to confirm and record ligamentous laxity or rupture (see Figure).



Valgus stress film with knee flexed 30 degrees. Consistent with rupture of medial collateral ligament.

Treatment

If a severe injury to any of the ligaments or to either of the menisci has occurred, hemarthrosis and effusion usually follow immediately. The quicker a bulky pressure dressing is applied, the less bleeding and effusion there will be. Aspiration of the joint is indicated both as a diagnostic aid and as a way of relieving discomfort; it should be done under strictly aseptic technique. If there is hemarthrosis, a tear of a ligament or mensicus has most probably occurred. If there are fat globules in the aspirate, a fracture has most probably been sustained. Decreasing the intra-articular pressure definitely affords relief of pain. Pressure dressing, elevation, and ice packing are deterrents to reaccumulation of blood and joint fluid. Should hemarthrosis reform, multiple aspirations are warranted in order to avoid the complications of protracted resorption of the blood, which leads to synovial reaction, formation of fibrin deposits, and adhesions.

In the case where a sprain has occurred and there is a possibility of internal derangement as well, a cylinder cast for 2½ to 3 weeks is indicated. This will allow soft tissue healing to take place with the knee immobilized, and the patient will be comfortable. He may bear full weight without fear of the knee hurting or buckling. Then, after motion has been regained following removal of the cast, further evaluation of the status of the menisci can be done. If the patient has either a locked knee or rupture of ligaments, surgical consultation concerning the advisability of meniscectomy and /or early surgical repair of the ligaments is certainly indicated.

Rehabilitation

An athlete should not be allowed to return to participation until there is no longer effusion present. He may be able to participate, but he will in most instances do damage to his knee if he engages in athletic activity while there is still effusion present. Rehabilitation consists of isometric progressive resistance exercises of the quadriceps, guarded and progressive weight bearing with crutches, and active range of motion exercises until full range of motion is achieved. The quadriceps of the injured knee should be at least as strong as — and preferably stronger than — those of the normal knee. If ligaments have been severely strained or torn, the knee should probably be protected with criss-cross taping during future competition.

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Imhotep

Imhotep (2980-2950) was an Egyptian priest and philosopher during the reign of Pharaoh Zoser. As priest familiar with magic and as philosopher conversant with natural law and physics, he was also, by extension, a physician, since in ancient civilizations magic and medicine were inseparable. Furthermore, 'physician' derives from 'physicien': a natural philosopher, an experimentalist in physics.

Because of Imhotep's phenomenal cures, shrines and temples rose in his honor, to which the ailing and afflicted pilgrimaged for his intercession. So exalted did his figure become that after his death, he was deified as the son of the god Ptah — one of only two Egyptian mortals so invested posthumously with divine paternity. The myth of immaculate conception has been indigenous to several ancient cultures; Christianity has not been the only institution to incorporate it into its doctrine.

For centuries Imhotep's shrines multiplied and continued as meccas, and his temples proliferated and flourished as medical centers. The most magnificent of these latter, that at Saqqara, was called the Asclepieium, since Imhotep was regarded as the Egyptian counterpart of the Greek Aesculapius. The Egyptian demigod physician is represented as a seated, shaven priest holding an open scroll on his knees.

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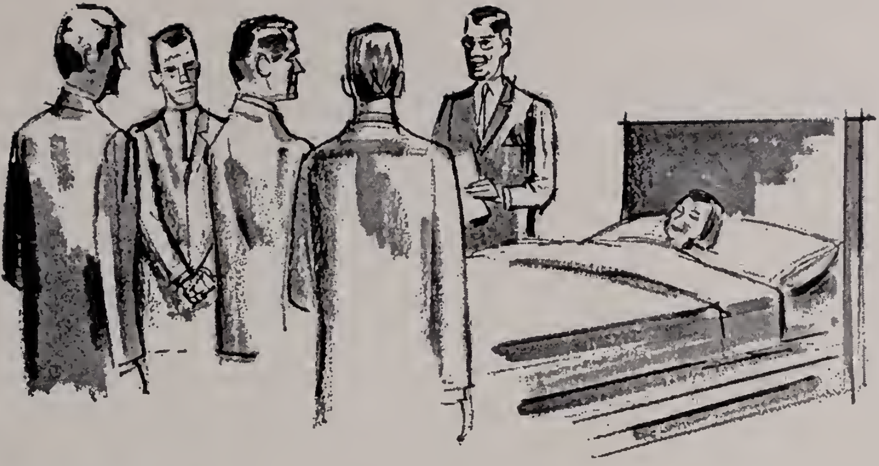

Grand Rounds

Thrombolytic Therapy*

The development of new means to control disease processes has resulted in a great increase in the number of persons in the older age groups. These older people have a higher incidence of diseases which cause or are associated with thrombotic disorders. Surgical treatment of these thrombotic complications is frequently not possible. Anticoagulants, while preventing in many cases further thrombosis, probably have little benefit in restoring circulation to the ischemic area. Anticoagulants are capable of preventing propagation of a thrombus once formed but cannot lyse the newly formed clot. Thus, the development of usable thrombolytic agents would be a major advance in the therapy of thrombo-embolic disease.

History

The term "fibrinolysis" was introduced for the first time in 1893 by Dastre, who used it to describe his observation that the blood of people who died a sudden death did not clot. It was mostly a descriptive concept until 1933, when Tillett stimulated further experimental investigation with his discovery that clots of human plasma would dissolve rapidly in the presence of filtrates of certain strains of hemolytic streptococci.[1] The substance in these filtrates has subsequently been identified as streptokinase (SK). In 1952, Johnson and Tillett first reported that infusion of high doses of streptokinase in rabbits produced partial lysis of 50 per cent of thrombi experimentally produced in ear veins.[2] In a series of experiments on animals Cliffton produced complete lysis of experimental thrombi in several different veins of a variety of animals without side effects.[2] The first reported experience of trials with plasmin infusion in humans was published in 1956.

Mechanisms

An understanding of the basic mechanisms of fibrin formation and

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*Presented as a Medical Grand Rounds at Mt. Sinai Hospital, Minneapolis, November 10, 1964.

Continued

fibrinolysis is important to the understanding of thrombolytic therapy. The whole process is a dynamic one, continually in action at numerous sites in the vascular system where stress and trauma occur. If the clots formed at these sites were not dissolved, life could not go on. The first three stages of the clotting mechanism are well known; but the fourth stage, that of fibrinolysis, has not received as much attention.[3,4]

Although the processes of coagulation and fibrinolysis are antagonistic, there are similarities in their mechanisms.[1] A proteolytic enzyme is produced by each system (thrombin and plasmin). Thrombin splits off a small particle (fibrinopeptide) from fibrinogen, while plasmin splits fibrin into a great many polypeptides. Both of the proteolytic enzymes are derived from an inactive precursor present in plasma. And finally, activation of the precursor to the active enzyme can be accomplished by either a tissue or a blood activator.

FIGURE I
Clotting and Fibrinolysis

Stage I	Platelets Antihemolytic factor Plasma thromboplastin Plasma thrombo antecedent Hageman factor	→	Plasma thromboplastin
Stage II	Plasma thromboplastin Prothrombin Calcium Limit of flocculation SF Stuart factor	→	Thrombin
Stage III	Thrombin Fibrinogen	→	Fibrin
Stage IV	Plasmin + activators	→	Plasmin
	Plasmin + fibrin	→	Fibrin is lysed into many polypeptides

Spontaneous Thrombolysis

Spontaneous thrombolysis is a biological phenomenon which has been observed and could be considered the antithesis of coagulation. It is both reproducible and predictable, and it indicates that there is a functioning homeostatic mechanism opposed to coagulation.[5,6]

Increased spontaneous thrombolysis has been reported[7] in obstetrical cases where there is a retained dead fetus or an embolism of amniotic fluid, and in cirrhosis of the liver. In these cases it may be due to a decrease in serum fibrinogen.[6] There are also reports of spontaneous thrombolysis following surgery, especially in thoracic procedures, in carcinoma of the prostate, in leukemia, after stress or exercise, in electric shock, in venous obstruction, and in injections of epinephrine, nicotinic acid, bacterial pyrogens and urokinase.[2,7] In these cases, no real decrease of fibrinogen has been reported.

Plasminogen (Proplasmin) and its Activators

Plasminogen is the inactive enzyme precursor of plasmin, forming plasmin by the splitting off of peptides.[7,8] It migrates with the serum globulins, has a molecular weight of 140,000, and is found both intravascularly and extravascularly and in certain body secretions. It is activated by a variety of substances: plasma activator in plasma, tissue activator in various tissues including blood vessels, bacterial activators such as streptokinase and staphylokinase; by other substances, among which are chloroform, acetone, alcohol and the pancreatic enzyme trypsin, and by activators present in some body fluids, notably urokinase, which is found in urine.[6,8] Of these activators, streptokinase has been the only one used extensively. It is now available in pure form, with only trace impurities, and is well tolerated in humans.

The presence of activators, such as urokinase, in certain body secretions, and similar activators found in milk and tears, have suggested that these represent excretion forms of the circulating activators. They may serve a useful purpose by preventing the formation of coagula which would obstruct the excretory ducts.[1]

Various tissues have been analyzed for the presence of tissue activator; the concentration has been found to be highest in the prostate, meninges and thyroid gland.[1] Prostatic carcinoma may result in spontaneous thrombolytic activity.

It seems probable that the activator substance(s) is derived from a proactivator, but there is little experimental support of this at present.

Plasmin[7,8] ("Fibrinolysin")

This is the active fibrinolytic enzyme and has a molecular weight of 108,000. It is a proteolytic enzyme (protease) of the trypsin class and resembles trypsin especially as to the type of linkage which it splits, and the pH optimum. It has rather nonspecific proteolytic ability in that it hydrolyzes, in addition to fibrin, fibrinogen, factors V and VIII, proaccelerin, AHF, some components of complement, ACTH, STH, glucagon, prothrombin, Christmas factor, and certain other blood proteins. It also hydrolyzes casein, thus providing one of the methods for determination of plasmin activity in vitro.

Plasmin Inhibitors[1,8]

It is evident that with the nonspecific proteolytic ability of plasmin, there must be some inhibitor to prevent it from causing widespread hydrolysis in the body. Postulated plasmin inhibitors include two antiplasmins, an inhibitor of the blood activator, as antistreptokinase, and E-aminocaproic acid. E-aminocaproic acid has been shown to inhibit as well as activate plasmin, and has provided a method of controlling thrombolytic activity where infused plasmin is used as the thrombolytic agent. The antiplasmins have not been adequately characterized; but it is known that one is found within the $alpha_1$ globulin plasma fraction and another in the $alpha_2$ fraction. It is probable that one of these is a fast-acting inhibitor, while the other inhibits slowly. Platelets have also been found to contain antiplasmin.

Specificity of Plasmin for Fibrin

Since plasmin is capable of hydrolyzing such a large number of substrates, what accounts for its specificity for fibrin? Two main theories have been proposed and experimental evidence provided for their substantiation. The first, proposed by Ambrus and co-workers,[7] proposes the existence of a circulating plasmin-antiplasmin complex, with effective competition for plasmin by fibrin. They injected isotope-labelled plasmin

Continued

into dogs and observed an initial increase of fibrinolytic activity, which rapidly disappeared. Yet the level of radioactive isotope remained high, and experimental clots exposed to this blood were slowly lysed. This led to the conclusion that an inactive plasmin-antiplasmin complex had been formed, and that the fibrin was able to compete effectively with this complex for the plasmin, which then resulted in lysis. According to this theory, thrombolytic therapy would consist of adding active plasmin to the patient's blood, thus providing a high level of circulating complex and continual but slow lysis of thrombi. The main concern would be to infuse the plasmin slowly enough so that the whole thrombolytic system would not be thrown into a generalized state of proteolysis, an eventuality which could be avoided by the infusion instead of the plasmin-antiplasmin complex.

The other theory, developed by Sherry and workers[4,7] proposes that when a thrombus is formed, it incorporates or adsorbs some of the circulating plasminogen, and that this occurs because the physical characteristics of plasminogen are similar to those of fibrinogen and fibrin. When circulating plasminogen is activated to plasma, it is immediately tied up by antiplasmin; but as the adsorbed plasminogen is slowly activated, the antiplasmin cannot attach to it, and slow lysis of the thrombus results. According to this concept, the level of activator in the circulation is more critical than the level of circulating plasmin. Sherry, therefore, has taken the approach of infusing the activator streptokinase in his experiments.

Use of Streptokinase

Sherry[4] has found that the plasminogen adsorbed on to the fibrin clot cannot be activated until all of the circulating plasminogen has been activated by high levels of circulating streptokinase. It is necessary to first give a priming dose, and then maintenance doses, to achieve adequate thrombolysis. The priming dose results in a state of hyperplasminemia, reflected by about a 30% decrease in fibrinogen levels, and occasionally by a hemorrhage. Sherry was able to avoid this latter complication by simultaneous infusion of hydrocortisone. After a short time all of the plasmin is inactivated by antiplasmin, and exhaustion of circulating plasminogen occurs. Then the proteolytic state decreases. About two hours after the beginning of therapy, active clot lysis begins and is dependent on the maintenance of continuously high levels of circulating streptokinase

There are, then, two phases in the effect on the fibrinolytic system produced by infused streptokinase. The first phase is proteolytic and is short, lasting only one to three hours. During this time, plasminogen undergoes rapid and complete activation and free plasmin is liberated into the circulation. If blood is drawn from a patient during this period it will clot and then lyse because of circulating active plasmin. During the second or thrombolytic phase the concentration of the activator reaches a high level and is maintained. This period will last as long as the infusion of activator continues. Plasminogen remains depleted, and all free plasmin has been inactivated by antiplasmin. Blood drawn from the patient during this phase will clot, but it will not then lyse spontaneously, because the plasmin is completely inhibited and there is no supply of plasminogen for adsorption to the newly formed clot. Without adsorbed plasminogen, there can be no activation to plasmin and no subsequent lysis of the clot. A clot which was previously formed will lyse, nevertheless, due to the high level of streptokinase which activates the previously adsorbed plasminogen.

Sherry[7] was unable to demonstrate effective clot lysis in the absence of a high level of circulating activator; he therefore challenges the validity of Ambrus' theory, despite the experimental support provided by the latter. Sherry[4] states further that it is unlikely that purified plasmin preparations can be developed for systemic thrombolytic therapy because:

1. Plasmin in the circulation has very little effect on a preformed thrombus, since it cannot activate the intrinsic plasminogen.
2. If clotting should occur in the presence of free plasmin, the resulting clot will be digested by this proteolytic enzyme. This would be of only limited prophylactic importance.
3. The presence of an activator which can diffuse into the thrombus and activate the plasminogen from within is necessary.

A unified concept regarding the in vivo specificity of plasmin for fibrin would be of help in resolving this conflict. Perhaps both are correct or, more likely, both contain elements which approximate the underlying reality.

Disadvantages of Thrombolytic Therapy

It has been suggested by several investigators[7] that there would be certain disadvantages to the use of thrombolytic agents, especially in treatment as advocated by Sherry, which is more intensive than that of Ambrus, is more costly, and requires careful laboratory control.

A major problem appears to be formation of antibodies to streptokinase from previous exposure to streptococcal organisms. Retreatment would be especially difficult because increased amounts of streptokinase would have to be used to neutralize the antibodies, and hypersensitivity reactions might occur.

No cases of embolism as a complication of lysis of thrombi have been reported.

A syndrome resembling the "crush syndrome" was reported in one patient. The re-establishment of circulation in a necrotic limb appeared to result in the absorption of toxins systemically, causing shock and death.

Clinical Experience with Thrombolytic Therapy

A major difficulty in evaluating the results of thrombolytic therapy in humans is the inability to be certain of the exact cause of a vascular occlusion. Similar clinical findings may result from embolic occlusion of a vessel, thrombosis, occlusion due to atherosclerosis, or perhaps even from vessel spasm.

One investigator[9] treated twenty-three patients with various types of arterial and venous thrombo-embolic diseases, using plasmin. Fourteen were felt to be inadequately treated because the dosage schedule was suboptimal. Of the nine who were adequately treated, eight were improved; in the one who was not improved, the vessel had been occluded by an old organized embolus. In most cases treatment was instituted within twenty-four hours after onset of symptoms.

Another group of seventy-one patients were treated with plasmin, with special attention paid to side effects.[13] Fifty were being treated for acute or subacute thrombophlebitis of a lower extremity. Twenty-one had

Continued

a temperature rise of over two degrees attributed to the therapy; four had shaking chills; three had asymptomatic hypotension; two had symptomatic hypotension; five had nausea and vomiting, and three had facial flushing. The authors concluded that, in spite of the high incidence of hyperpyrexia, plasmin was safe and beneficial in the treatment of thrombophlebitis.

In one series of 197 patients treated with thrombolytic therapy[2] only four instances of hemorrhage were noted. There was only a minimal increase in the prothrombin time, and, although there was a decrease in the fibrinogen concentration in 50%, the lowering was not to critical levels, even after 12 to 24 hours of therapy.

Of the 197 cases, 98 were cases of venous thrombosis, and 36, of arterial thrombo-embolism. The results are tabulated as follows:

TABLE 1

Results of Fibrinolytic Therapy in 98 Cases of Venous Thrombosis[2]

Duration	No.	Improvement Good	Improvement Fair	Improvement None	Average Treatment (days)
Acute, 5 days	48	40	7	1	2.8
Five to14 days	17	13	1	3	3.5
More than 14 days	23	13	4	6	4.1
Tumor or mechanical obstruction	10	0	0	0	3.0

Twelve of the patients were treated for pulmonary emboli:

Result	No.
Excellent	8
Good	1
Death	3

TABLE 2

Results of Various Types of Therapy in 36 Cases of Arterial Thromboembolism[2]

Time and Treatment	Total	Results Good	Results Improved	Results No Change
Prior to 1958	6	0	0	6
Since 1958				
Systemic only	17	5	4	3
Local only	7	4	0	3
Fibrinolysin plus femoral embolectomy	6	4	1	1

Thrombolytic agents have been advantageously used in conjunction with heparin.[11] It was found that there was no antagonism between the drugs and no increased incidence of hemorrhage over that which would have been expected with heparin therapy alone. The investigators felt that they had prevented the recurrent venous thrombosis experienced with earlier trials on thrombolytic therapy alone.

Experience with the use of thrombolytic agents in the treatment of acute myocardial infarction and cerebrovascular accidents is limited. A problem in the treatment of the acute myocardial infarction is that in 40 per cent there is no evidence of a fresh thrombus.[10,12] One investigator[12] treated forty-five patients with acute myocardial infarction with thrombolytic agents followed by treatment with anticoagulants. Thirty-nine survived and six died. It is still too early to draw any conclusions as to the clinical value of thrombolytic therapy in the stroke syndrome, but investigation in this regard is under way.

Case Report

A 43-year-old white man was transferred to Mount Sinai Hospital from another hospital on October 29, 1964. He had been admitted to the other hospital 10 days previously because of the sudden onset of severe shortness of breath without chest pain. This occurred while playing golf. Over a two-year period he had noticed a moderate increase in shortness of breath with exertion; however, he had otherwise felt well and had no symptoms. There had been no history of thrombophlebitis or heart disease. Before transfer to Mount Sinai Hospital he had been treated for right heart failure.

Physical examination on admission to Mount Sinai Hospital revealed a well developed and well nourished white male who was having moderate shortness of breath at rest. There was cyanosis present and the patient was orthopneic. The neck veins were markedly distended. Blood pressure was 120/80, pulse 86 and regular. The lungs were clear to percussion and auscultation. A friction rub was not heard. The heart was moderately enlarged to right and left and a presystolic gallop rhythm was present. The pulmonic second sound was louder than the aortic second sound. The liver was palpable to three fingerbreadths below the right costal margin. There were no masses in the abdomen and no ascites. There was minimal edema of the lower legs. Peripheral pulses were normal.

A chest X ray revealed decreased lung markings over the right lung compared to the left. Shortly after admission to the hospital a pulmonary angiogram was performed and revealed a complete block of the right pulmonary artery and poor filling of the left pulmonary artery.

At this time, because of the demonstrated block in the pulmonary circulation despite the history of 10 days since the onset of symptoms, it was felt that surgical exploration of the pulmonary arteries and an attempt at removal of any large thrombi was indicated. On October 30, 1964, a surgical pulmonary embolectomy was performed and multiple emboli were removed from both pulmonary arteries. However, during surgery the patient went into severe acute right heart failure and expired shortly after the surgery was completed.

Although thrombolytic therapy was not undertaken in this patient, it was considered, and if he had survived the immediate postoperative period, thrombolytic medical therapy would have been instituted. If an established effective form of thrombolytic therapy were available, surgical exploration in this patient might have been avoided.

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WHAT WE DID (see page 1350)

The rosary was grasped through the esophagoscope and brought to the area of the cricopharyngeal muscle. However, at this point it caught, and cervical esophagostomy was required for the removal. The patient recovered without further complications from this incident.

Jean R. Eckerly, M.D.
George E. Kitzmiller, M.D.
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Nonmetallic Implants

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NONMETALLIC IMPLANTS apparently were used for the repair of various bony defects at the time of earliest recorded history. Transplantation of bone from lower animals to injured humans is recorded in the medical writings of early Hindu, Egyptian, and Greek civilizations. Heterologous bone transplantation was apparently used quite extensively in the eighteenth and particularly in the early part of the nineteenth century. According to standard orthopedic reference books,[1] ivory seems to have been the first material other than heterologous bone used extensively with any degree of success. In 1884 Ogston performed a talonavicular arthrodesis for flat feet, apparently by using an ivory peg as a bone block, and in 1886 Bircher advocated the use of ivory for grafting because he thought it more "resistant" than heterologous bone. However, the predictably successful use of grafting had to await the development of strict antisepsis in graft preparation and in surgical technique.

Experience in both world wars demonstrated the need for materials which could be used as internal substitutes for body tissues, particularly in vascular and massive bony injuries. There was a marked increase in the use of autogenous grafting. Coincident with these developments, organic chemists were making rapid strides in the production of a great variety of stable polymers or plastics, a few of which have at least partially met the majority of physiologic and mechanical requirements for successful human implantation.

Definitions

In a fine review article published in 1960, Urist[2] clarified the meaning of a number of terms which have been used more or less interchangeably in much of the literature pertaining to this subject. A good deal of confusion can be eliminated if the following definitions are kept in mind.

Transplant or Graft

An autologous, autogenous, or isogenous sample of donor tissue that contains viable cells with the capacity for survival and growth in a new location without antigenic response.

Tissue Transfer

A term used to describe *fresh* homografts or heterografts because it is noncommittal with respect to cell viability and donor tissue survival.

Tissue Implant

Connotes nonviable, coagulated, frozen, or denatured tissue that does not contain cells having the capacity to proliferate or produce new tissue.

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Tissue Derivative

This implies tissue from which one or more components, such as mineral, water, ground substance, protein, or lipid, have been removed.

Tissue Substitute

A synthetic material which is foreign to the body and which is introduced to function temporarily or permanently as a tissue, splint, or prosthesis.

In accord with these definitions, nonmetallic implants may be broadly defined as any materials other than metallic devices and autogenous bone, which are surgically placed within the body.

Criteria for Nonautogenous Materials[3]

To be *suitable*, a material: (1) must not produce inflammation or foreign body reaction; (2) must not elicit any stage of allergy or hypersensitivity reaction; (3) must resist mechanical strains secondary to the purpose for which the prosthesis was designed; (4) must be sterilizable; (5) must be noncarcinogenic; (6) must be amenable to fabrication in the desired form; (7) must not be physically modified by surrounding tissue; and (8) must be chemically inert. Criteria 7 and 8 have no application to bone implants (homogenous and heterologous) and bone derivatives, because the essential feature of their function appears to be their ability to act as a lattice for formation of new bone while they are simultaneously destroyed and absorbed by the host.

The major *obstacles* to the use of exogenous materials as implants include: (1) antigenicity and rejection; (2) foreign body reactions; (3) loss of substance or function; (4) infections; and (5) inadequate knowledge of final fate of implants and of possible metabolic, mechanical, and hyperplastic side effects.

Specific Materials

The discussion will be generally limited to those materials which have been proposed for some use in orthopedics, particularly as graft substitutes for autogenous bone.

Tissue Transfer

Fresh Homogenous Bone — The only application for the use of fresh bone from another individual of the same species is transfer between identical twins. Limitations on the use of this procedure are obvious.

Fresh Heterologous Bone — There is essentially no clinical or investigative interest now because of antigenicity and graft rejection.

Fresh Embryonic Bone — Only temporary graft survival can be expected and little practical use for such bone has been demonstrated.

Tissue Implant and Tissue Derivative

The materials classified under this heading are homogenous bone and heterologous bone which have been treated in one of a variety of ways in order to produce sterility as well as minimal or no antigenicity for grafting purposes. These categories will be considered together because of the difficulty in deciding whether bone tissue has only had its protein denatured or whether a portion of the osseous material has actually been extracted in the preparation.

Homogenous Bone — This is human bone used to stock bone banks. The following treatments have been utilized and found successful, at least experimentally, in the preparation of homogenous bone for use in grafting: refrigerated at 2 C; refrigerated in 0.9% saline at −5 C; frozen at −30 C; freeze-dried; coagulated with thimerosal (Merthiolate) solutions; sterilized and preserved by hydrogen peroxide; sterilized and preserved by beta-propiolactone solutions; and sterilized and preserved by boiling in glycerol and water.

Heterologous Bone — Long-standing interest in the use of heterologous bone as a substitute for human bone in grafting has been mentioned. Recently, clinical interest in this type of bone implant has been heightened by the introduction of a material called "processed heterologous bone."*

The experimental basis for the clinical use of this material in the United States was provided by Karges and co-workers.[4] Using macroscopic, histologic, tetracycline fluorescence, and microradiographic techniques, they showed that processed heterologous calf bone behaved biologically comparable to fresh autogenous bone in the process of host incorporation and remodeling of bone implants. There were two exceptions to this generalization. The first was that fresh autogenous bone took up mineral rapidly during the first two weeks, whereas the heterologous bone did not; however, after one month there was no appreciable difference in mineralization between the two types. The second exception was that there was more remodeling of the cortical heterograft than of the cortical autograft at six months. They concluded that:

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*Boplant, E. R. Squibb & Sons.

"Evidence indicates that antigenicity of the calf-bone heterograft has been lowered effectively without adversely altering its structural characteristics. This, in conjunction with effective eradication of cellular debris from the large trabecular and macrocanalicular spaces and negligible fat content in the calf-bone heterograft, has enhanced its effectiveness as a bone transplant to compare favorably with the autograft."

Processed Heterologous Bone

Primarily on the basis of this experimental evidence, Anderson and co-workers[5] proceeded to use processed heterologous bone clinically. They did 452 grafting procedures and had a follow-up of more than six months on 351 patients. They reported the infection rate as 1.3% and successful graft rate as 85%. In spite of the difficulties inherent in determining nonunion and the bias of clinical authors evaluating their own results, it would seem that these results compare favorably with those in other series in which homografts and autografts were used.

Advantages

According to the manufacturer, processed heterologous bone offers a number of advantages:

1. The problems of antigenicity, failure of graft assimilation, and sterility have been solved.
2. Lyophilization* and packaging in partial vacuum have rendered the material easily transportable and available as well as enabling storage at room temperature.
3. This material provides wide and open marrow spaces for invasion by blood vessels of the host.
4. The mechanical stability of this type of implant equals that of autogenous bone.
5. The problems of an insufficient autogenous bone supply for some procedures and of creation of a painful donor site are eliminated.
6. Operative infection rate is as low as that found with use of autogenous bone and lower than that found with use of homogenous bone.
7. The problems of bone-bank-processing, bacteriologic control, provision of the proper type of bone, and medicolegal considerations are eliminated.
8. Average costs of equal amounts of homogenous bone and processed heterologous bone in some institutions are $150 and $30, respectively.

From these glowing reports, one could surmise that an almost ideal substance for bone grafting has been found. However, such a conclusion is premature until more extensive clinical experience with long-term follow-up is gained.

It should be mentioned that other methods of preparation of heterologous bone have been used with at least some degree of success. These include complete freezing,[6] autoclaving,[7] and defatting with sterilization in alcohol solutions.[8] These methods all produce protein denaturation and hence decreased antigenicity; but they have not been brought to the apparent level of sophistication and mass production found in the Squibb process.

Bone Derivatives

Bone derivatives made by treatment with various other chemicals to remove specific components of bone have been used as implants in experimental situations. The purpose of these methods is to produce a substance which has decreased antigenicity or which is more rapidly absorbed by the host, compared to autogenous, homogenous, or heterologous bone. *Decalcified bone* is made

Continued

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*See Test Your Word Score Page 1333.

by extraction with either acid or ethylenediaminetetra-acetate (Versene).[9] *Deproteinized bone* is the result of treatment with ethylenediamine[10] or hydrogen peroxide,[11] which removes most of both collagenous and noncollagenous (protein?) material of bone. This derivative apparently is not well vascularized and has little mechanical strength.[12] *Collapatite*[13] and *os purum*[14] are derived from bone by extraction with urea-8.8% saline or potassium hydroxide, respectively. Collapatite ("collagen and hydroxyapatite") is an inert, hard substance with a microcanalicular system which is replaced more slowly than that of bone and apparently is the product of extraction of intracellular proteins and mucoproteins. Both of these materials have been recommended as substitutes for internal fixation but not for filling bone defects.

Tissue Substitutes

Orthopedists with a taste for science fiction should be interested in McFarland's[15] speculations written 15 years ago. Writing as of the year 2000 A.D., he commented on the ever increasing number of injuries resulting from the general use of helicopters:

> "Fortunately, this increase in the frequency of bone fractures has been unimportant because intramedullary fixation with thermoplastic, homoplastic agents injected directly into the fracture site, cancellous in their form, setting to the resilience and strength of steel, stimulating callus formation, and being resorbed in that process, has permitted weight-bearing in nearly every fracture."

Quigley[16] suggested that the present state of knowledge regarding the use of organic polymers or plastics is similar to that which prevailed regarding the use of metals in the early part of the twentieth century when the fundamental principles of mechanics and electrolysis were not appreciated. Although there has been a remarkable increase in the study of the surgical applications of these materials, with few exceptions none seems to offer advantages over more traditional treatments. On the contrary, it seems that there is a general state of confusion about indications for orthopedic use of implant plastics, and many human implantation experiments have ended disastrously.

The following substances have received substantial clinical trial.

Polyurethane (Ostamer)

The initial reaction of a monomer of urethane with a catalyst forms a liquid material which is then poured into a bony defect; it hardens in 15 to 20 minutes into a rigid, spongelike material due to the liberation of CO_2 during polymerization. When the use of polyurethane was first proposed by Salvatore and Mandarino[17,18] in 1959, it seemed that McFarland's speculations might be coming true, because the material was advertised as having enough strength and cohesiveness to permit almost immediate weight bearing, as being nontoxic, as promoting osteogenesis, and as being easy to handle. Subsequent studies by other investigators[19,20] have failed to substantiate these claims.

Methyl Methacrylate or Acrylic (Lucite)

This material has become familiar to orthopedists because of its initial use in the Judet hip prosthesis.[21] Primarily because of its tendency to fracture and erode, it has been discarded for prosthetic uses and is now used primarily to fill skull defects[22] and for dentures.[23] It has been tried, unsuccessfully, as a hip mold.

Tetrafluoroethylene (Teflon)

The successful use of Teflon fibers woven or knitted into fabrics as protheses for the aorta and large vessels is well known. It is the most chemically inert substance for implantation now known. Charnley[24] has devised a hip arthroplasty which utilizes a precast Teflon socket with deep serrations on its outer surface and a ⅞-inch prosthetic head. Walldius[25] has implanted a metal knee-prosthesis with a Teflon layer over its articular portions in 64 arthritic knees; results were classified as good in 64% of cases. Teflon was used in prosthesis construction because of its low coefficient of friction and its resistance to mechanical abuse. It has been used unsuccessfully as a tendon and tendon-pulley substitute in dogs.[26]

Silicones (Silastic)

The chemical structure of these materials consists of long chains of silicon and oxygen atoms in alternation and resembles that of natural rubber, plastics, and oils which are made up of long chains of carbon atoms. They are produced as fluids of varying viscosities or as rubbers which have varying strengths and elasticity. Room-temperature-vulcanizing (RTV) silicone rubbers utilize stannous octoate as a catalyst. The advantage of this material is that it can be injected or poured, with its catalyst, into a soft-tissue defect and it will cure in situ. The silicones are heat stable, are unaffected by time, do not adhere, and do not induce tissue reactions.

Silicones have been used primarily in plastic surgery in such diverse ways as breast and facial tissue augmentation and prevention of readhesion after separating bony temporomandibular ankylosis or prevention of premature fusion in craniosynostosis. RTV silicone polymer has been poured around aneurysms of the circle of Willis; 40,000 Holter valves have been implanted as permanent drains for hydrocephalus. It is used routinely in operations for detached retinas and as a replacement for vitreous humor. The most widely used prosthetic heart valve (Starr-Edwards) utilizes a silicone-rubber ball. In orthopedics, this group of materials has been used as a sheathing to prevent adhesions after tendon graft, as a matrix for the creation of new autogenous tendon sheaths, as direct artificial implants for tendons, and in the prevention of readhesion following release of radioulnar synostosis. It seems safe to predict that many more uses will be found for these compounds because of their inertness and physical versatility.

Other Plastics and Polymers

These have received substantial experimental evaluation but in general seem to have little potential for orthopedic uses. *Polyvinyl alcohols* (Ivalon) have been tested as orbital[27] and breast[28] implants; they seem to provoke a dense fibroblastic response. *Polyethers* (Etheron) also have been implanted as tissue augmenters.[28] *Polyethylenes* (Marlex) have been fabricated into porous, strong materials which have been implanted for tracheal reconstruction.[29] *Coal-tar derivatives* (nylon) are well known as suture materials; they were used briefly and with very undesirable results in hip[30] and knee[31] prostheses in the early 1950s and, more recently, have been fabricated into a mesh incorporating a cellulosic material (Millipore-Microweb)[32] for use (with encouraging results) as a filter allowing tissue fluid diffusion but not fibroblastic infiltration into tendon anastomoses. *Cellulose derivatives* (cellophane) have also been used as a sheathing material after synovectomies and section of synostoses. *Polyesters* (Dacron), another familiar type of polymer, have been used as fabric for vascular prostheses. Starch sponge has been tested as bone filler.[33]

Plaster of Paris

Peltier[34] claimed excellent success with use of sterile gypsum (the hemihydrate of $CaSO_4$) as an implant for filling large bony defects. The plaster of Paris is absorbed simultaneously with new bone formation, does not seem to interfere with or promote osteogenesis, and seems to act as a filler to retard fibroblastic infiltration while osteogenesis proceeds. Peltier presented 20 healed cases in which this implant material was used, even in the presence of infection.

Ceramic-Epoxys

A mixture of alumina, silica, calcium carbonate, and magnesium carbonate heated at 2,700 F. produces a true interconnecting-porosity ceramic. When this material is impregnated with an epoxy resin, a lightweight, inert material, as strong as bone and with bone's elasticity, is produced. This material has been suggested as a bone substitute.[35]

Modified Protein (Bioplast)

This is an absorbable material made by compressing fibrin under high pressure. The material is molded and used as a cup for hip arthroplasties in the treatment of tuberculo-

Continued

sis. According to its proponents,[36] it should be used in joints that show minimal destruction after two to three months of antituberculosis chemotherapy. The material is apparently neutral to tuberculosis, does not stimulate tissue reaction and, since it is subject to proteolytic breakdown in three weeks to eight months, serves as a temporary protective device to allow cartilage regeneration. Residual hip stiffness has apparently been a problem.

Gelatin — This animal protein derivative has also been tested as a bone filler.[37,38]

Summary and Conclusions

One can easily surmise from this brief report that the subject of nonmetallic implants is an expanding and promising field. Medical research has produced several materials that have wide clinical application. Results of preliminary testing with processed heterologous bone (Boplant) are encouraging, and the material seems to compare favorably with autogenous bone for grafting. The plastics, particularly Teflon and the silicones, have found uses in a variety of surgical problems but, with the possible exception of tendon surgery, offer no advantage over metallic implants or traditional procedures in orthopedics. Despite the failure of polyurethane (Ostamer) it seems that the realization of McFarland's predictions may come in the not so distant future.

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7-38 May be obtained from the author or the reprints.

The Tobacco Tyrant

There are two schools within the medical profession on the effects of the use of tobacco on the human economy. Were it not for the fact that members of our profession are among the chief devotees of the weed, the chances are, I believe, that there would be but one school of thought on the question, and that this thought would be told and expounded in a broader and more energetic manner than it is today. As proof of the evil effects of tobacco on the human system, I herewith present abstracts from literature on the subject, recorded by reputable and representative men of the medical profession:

Gould's Medical Dictionary puts it this way: "Tobacco is a plant, Nicotiana Tabaccum, the dried leaves of which contain a liquid alkaloid, Nicotine. Nicotine is one of the most active poisons known. Tobacco smoke contains a series of bases, among which are pyridine, picoline, lutidin, and others. Tobacco is used as a sedative in nearly all parts of the world, being smoked, chewed, or used as snuff. Its physiological action is that of a nauseant, antispasmodic and depressant. It is also a local irritant."

To be continued next issue.

E. O. Giere, M.D.*
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**Editors Note:* *This is a somewhat belated publication. In 1928 Dr. E. O. Giere, M.D. prepared and presented a manuscript at one of the Twin City hospitals on the evil effects of tobacco.*

Through the courtesy of his sons, Richard and Joe Giere, the timeworn and faded manuscript was made available to the editor. The contents seem more pertinent today than they were in 1928 when the manuscript was written.

Abstracts, Briefs and Commentaries

GASTRIC HYPOTHERMIA FOR DUODENAL ULCER

The medical literature indicates that gastric hypothermia for duodenal ulcer has not proven to be wholly successful, though approximately 50 per cent have continued to remain asymptomatic after one year. Repeated freezings have been used to control recurrent symptoms. The authors who indicate that the gastric mucosa temperature is usually not decreased below 0° C. may prefer to use the term gastric hypothermia in preference to gastric freezing.

The authors analyzed three groups of patients on the basis of the inflow-outflow temperature ranges. They observed the depression of the free hydrochloric acid, the X pepsin excretion and the clinical response in each of these three temperature categories.

In the cold group with the outflow of $-14.1°$ C. the results were best, showing excellent in 100 per cent after nine months. In the intermediate group with the outflow temperature of $-12.8°$ C. there were 33% presenting excellent results, and in the warm group with a temperature of $-11.1°$C. there were no excellent results at the end of twelve months.

These authors were able to conclude that gastric hypothermia is not a cure-all; nor is it worthless in the treatment of duodenal ulcer. They considered that the majority of patients can expect some benefit providing the temperature of the gastric mucosa is sufficiently depressed. They also indicated that there is a direct relationship between the degree of temperature depression and the decrease in the basal gastric acid and an increase in the X pepsin excretion and over-all beneficial clinical effectiveness. The colder temperatures provided the best results.

Though there are a few enthusiastic proponents of gastric hypothermia for duodenal ulcer, the preponderance of physicians are willing to await more definite evidence favorable to gastric hypothermia before adopting it as the accepted method of treatment for duodenal ulcer.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Rider, J. Alfred, M.D., Moeller, Hugo C., M.D. & Puletti, Ernesto J., M.D.: Use of Gastric Hypothermia in Treatment of Duodenal Ulcer. Arch Int Med 115:459, 1965.

OPERATIVE TREATMENT OF ADENOCARCINOMA OF THE ENDOMETRIUM IN OBESE WOMEN

Among 486 women who received primary treatment for adenocarcinoma of the endometrium at University of Minnesota Hospitals between 1939 and 1963, 98 (20.2%) weighed 200 pounds or more and were classified as obese. Five weighed more than 300 pounds, and one over 400. There was no significant difference between the obese and nonobese groups in age or parity. About 30% were nulliparous. Of the obese group 65% were evaluated for abnormal carbohydrate metabolism; of these, 52% exhibited some evidence of clinical or latent diabetes.

Although the mode of therapy during this time period was changed periodically to conform to a long-term planned program of treatment to determine the effect of radiation therapy in the treatment of this disease, total hysterectomy with bilateral removal of the adnexa was performed as frequently as possible as complete or partial treatment in both the obese and the nonobese groups. When surgical removal of the uterus and adnexa constituted partial treatment, preoperative intracavitary radium with or without external radiation therapy was also given.

Of the 98 obese patients, 88 (90%) underwent operative treatment with only three (3.4%) operative deaths. Abdominal total hysterectomy with removal of the adnexa was performed in 77 patients. Five of the remainder underwent vaginal hysterectomy, one radical hysterectomy, and five were deemed inoperable at exploratory laparotomy.

When the results of therapy among these obese patients were compared with the results among the nonobese who received the same therapy, the five, ten, 15, and 20-year survival rates among the obese women were equal to or better than among the nonobese. The total five-year survival rate among obese women was 65%. Of those who did not survive five years 17% died of recurrent disease, 9% had untreatable disease when first seen or refused treatment, and 6.5% died of causes unrelated to endometrial cancer.

This summary of operative treatment of adenocarcinoma of the endometrium demonstrates that obesity alone should not be a deterrent to operative attack upon the disease. The results reported were achieved with little attempt at preoperative weight reduction and no compromise in the mode of therapy. The 90% surgical and the 3.4% surgical mortality rates compare with 70% and 4% surgical and surgical mortality rates considered usual and acceptable when all patients with this disease are considered, regardless of weight. The authors attribute the results in this series to detailed preoperative evaluation of the general health status of the obese individual, careful surgical technique, and meticulous postoperative management.

Konald Prem, M.D.
Minneapolis, Minnesota

Reference

1. Prem, K. A., Mensheha, N. M., and McKelvey, J. L.: Operative Treatment of Adenocarcinoma of the Endometrium in Obese Women. Amer J Obstet Gynec 92:16, 1965.

PREVENTION OF PYELONEPHRITIS BY WATER DIURESIS

The medulla of the kidney has been shown to be more susceptible to infection than the cortex. The authors contend that at least a part of this vulnerability is due to the hypertonicity of the renal medulla.

They were able to induce a chronic water diuresis in female Sprague-Dawley rats by simply adding 5% glucose to their drinking water. Injections of laboratory strains of Candida albicans and Staphylococcus aureus were given intravenously to diuresing and normal control animals. These strains are known to cause infections of the renal medulla of normal rats. The animals were sacrificed at varying times up to eight days after inoculation. Urine cultures, cultures of homogenized kidney tissue, and histological sections were studied. In addition, spleens, livers, and blood were cultured and studied microscopically.

Water intake increased several fold without affecting blood sugar or causing glycosuria. Urine from experimental animals had low osmolarity and higher pH (mean value 7.88 as compared to 7.14 for control animals).

Sixteen of seventeen controls receiving Candida injections had pyelonephritis when sacrificed eight days later. Only three of seventeen experimentals had positive cultures, and none of these had the gross abscesses commonly seen in the controls.

Twenty of twenty-one controls receiving Staphylococcus developed pyelonephritis. When diuresis was begun one day before injection, only three of twelve animals were infected; when diuresis was begun one day after injection, only four of twelve animals were infected.

When Staphylococcus-treated animals were started on diuresis as much as three days after injection, six of thirteen animals were infected when sacrificed five days later. Since renal infections and abscess formation occur between 24 and 48 hours after injection of this strain, some of these rats must have been cured of their infection. Renal infection was not prevented or cured by three days of diuresis when it was started five days after injection.

Staphylococcus never appeared in the urine of animals undergoing diuresis, indicating that the organisms were not simply "washed out." In vitro studies demonstrated no bactericidal substance in renal medulla extracts from experimental animals.

These studies demonstrate that Candida and Staphylococcus renal parenchymal infections can be prevented, and suggest that Staphyloccal renal infections can be cured by decreasing the hypertonic environment of the renal medulla through sustained water diuresis.

Concentrated urine and saline solutions are known to inhibit phagocytosis. More dilute urine does not.

Hypertonic solutions have also been shown to inhibit the action of complement. Complement, lysozyme, and antibodies are known to injure the cell walls of urinary pathogens, causing the formation of protoplasts, which are lysed in isotonic or hypotonic environments, but preserved in hypertonic solutions.

Water diuresis induces an increased renal blood flow, which may play a part in the delivery to the kidney of more phagocytes and increased amounts of serum factors involved in body defenses.

The authors feel that this study "provides an experimental rationale for

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the time-honored practice of 'forcing fluids' in patients with urinary infection."

Fred Mecklenburg, M.D.
University of Minnesota

Reference

1. Andriole, Vincent T., and Epstein, Franklin H.: Prevention of Pyelonephritis by Water Diuresis: Evidence for the Role of Medullary Hypertonicity in Promotion Renal Infection. J Clin Invest 44:73, 1965.

TOXICITY OF SODIUM BISULFITE IN PERITONEAL DIALYSIS SOLUTIONS

Toxic symptoms typical of central nervous system stimulation were observed in using certain peritoneal dialysis fluids according to scientists at the University of Michigan. Sodium bisulfite was the causative agent.

The dialysis solution was prepared by a commonly used formula and contained 7% dextrose, 0.62% sodium chloride, 0.39% sodium lactate, 0.026% calcium chloride, 0.015% magnesium chloride, and 0.05% sodium bisulfite. Control data revealed no reason for the toxicity. During investigation of the formula, the authors found that the amount of sodium bisulfite was unusually high, based on the volume of fluid which may be used (10 to 12 liters in 24 hours). Consequently, if appreciable absorption occurred from the dialysis fluid, this quantity of bisulfite (500 mg. per liter) could be dangerous.

Sodium bisulfate is used to prevent discoloration of dextrose (and other items) in various solutions and may be used in concentrations up to 0.31%. However, these solutions are not administered in amounts as large as those used for peritoneal dialysis.

To evaluate the absorption, tissue distribution, and urinary excretion, S^{35}-labeled sodium bisulfite was used in the dialysis fluid and it was injected intraperitoneally into rabbits. Blood-level measurements showed that the bisulfite was absorbed rapidly from the dialysis fluid with the rate decreasing as the blood level increased. Some elimination of bisulfite was effected by urinary excretion and also by oxidation to sulfate. However, these mechanisms are limited and proceed too slowly or almost cease entirely, while absorption continues at a faster rate than elimination. Therefore, an accumulation of bisulfite in the tissues occurs, and if a sufficient concentration is reached, the central nervous system is affected and cardiovascular collapse results.

The authors conclude that, although the testing thus far is limited, the results do show that bisulfite should be greatly limited or excluded entirely from the final product.

They suggest that some bisulfite is oxidized to sulfate during manufacture. If an amount could be added which would be sufficient to protect the dextrose, but which would be almost completely utilized during processing, the limit on bisulfite content could be placed on the final product. Then it would not be necessary to eliminate bisulfite entirely, since an amount would not be present which might prove hazardous to the patient.

Halaby, S. F., and Mattocks, A. M.: J Pharm Sci 54:52, 1965.

CLINICAL ASPECTS OF BENIGN PROTEINURIA

Proteinurias identified as benign may have several causes. The author calls attention to an orthostatic form that occurs chiefly in young persons, in some while they are standing or walking, in others only after they assume a lordotic posture. Benign proteinuria also occurs after great physical exertion either in the form of exercises (sport activities) or of hard physical labor. Excitement or exposure to cold likewise may bring on reversible, benign proteinuria. Discussing the mechanism involved in these forms of proteinuria, the author suggests a common etiological process. While the proteinuria that characterizes congestive heart failure is probably the result of increased pressure in renal veins, this cause plays no part in benign proteinuria. The importance of slight structural changes in the glomeruli is questioned. The author describes observations on four adolescents with benign persistent proteinuria. The condition was not related to posture, and the findings on clinical examination and clearance tests were normal. Percutaneous renal biopsies likewise revealed no abnormalities. The author stresses, however, that the diagnosis of benign proteinuria should be made only after the exclusion of pathological conditions, and these patients should be kept under observation for long periods.

Courtesy of References and Reviews
Journal of the American Medical Association

Kleinschmidt, A.: Deutsch Med Wschr 88:2283, 1963.

REMINISCING IN THE AGED

Reminiscing, the habit of relating past experiences, was studied in 25 noninstitutionalized Spanish-American War veterans between the ages of 78 and 90. The tendency to reminisce was compared in each subject with (a) the degree of intellectual deterioration, (b) the presence or absence of depression, and (c) two-year survival after the interview. Findings suggest a positive correlation between the tendency to reminisce and freedom from depression and survival since the interview. It was not related to intellectual deterioration. There is a discussion of factors which favor reminiscing behavior as well as some of the psychological meanings of reminiscence and some ways in which it contributes to successful adaptation to senescence.

Courtesy of References and Reviews
Journal of the American Medical Association

McMahon, A. W., Rhudick, P. J.: Arch Gen Psychiat 10:292, 1964.

PHYSICAL EXERCISE IN BREATHLESS SUBJECTS WITH PULMONARY EMPHYSEMA

Breathlessness on exertion limits the physical activity of patients with severe pulmonary emphysema to such an extent as to result in physical unfitness and muscle atrophy. Oxygen inhalation during a graded exercise program overcomes this handicap in some cases. In many others, restoration of diaphragmatic function during walking is required even with the use of oxygen. The technique of breathing training required for effective use of oxygen-supported exercise is described. Elimination of a disordered

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breathing pattern in patients with obstructive pulmonary emphysema is shown to result in a more effective alveolar ventilation, and a consequent increase in the capacity for exertion. If tobacco smoke does not enter the lungs, the question is propounded: is there justification for an adamant position in respect to rejection of cigarette smoking.

Courtesy of References and Reviews
Journal of the American Medical Association

Barach, A. L.: Dis Chest 45:113, 1964.

ULCERATIVE COLITIS AND REGIONAL ENTERITIS

A review of surgical specimens from 57 cases of ulcerative colitis showed 35% to have involvement of the ileum. Eighteen cases of regional enteritis were also reviewed and 22% of these had involvement of the colon. These two disease entities were found to be distinct and distinguishable from each other regardless of the segment of intestine involved; the lesions of ulcerative colitis were primarily of the mucosa while those of regional enteritis were primarily of the submucosa and subserosa. The morphological differences between these two diseases and the rarity of their occurring together in the same patient are strong evidence against these diseases sharing a common etiology. Diagnosis and treatment should be based on the principle that these two diseases are distinct and distinguishable, regardless of the segment of intestine involved.

Courtesy of References and Reviews
Journal of the American Medical Association

Saltzstein, S. L., and Rosenberg, B. F.: Amer J Clin Path 40:610, 1963.

The Horus Eye

In ancient Egypt the udjat-eye (Horus Eye) was a sacred symbol of healing and medicine — corresponding to the familiar caduceus of today's medical profession.

The Horus Eye derives from the myth of Osiris, the sun god, who was killed by his brother, Set, and avenged by his son Horus. While engaged in slaughtering Set in reprisal for Osiris' murder, Horus suffered irreparable damage to one eye; however, the god Thoth miraculously restored it by spitting upon it. Not only did the eye completely recover; it was henceforth exalted to divine status as possessing magical curative properties.

Conventionally the Horus Eye consists of an eye within an equilateral triangle based like a pyramid — with Osirian sun rays emanating from all sides.

So vitally imbued with the Osiris myth was the ancient culture of the Nile that the Horus Eye became a popular pattern for therapeutic amulets, some of which, handsomely wrought of faience and jewels, can be seen in modern museum exhibits of early Egyptian art.

Even today the Horus Eye appears in modified character on some medical prescription forms and in some drug stores. Furthermore, its original significance either forgotten or ignored, the Eye makes a nontherapeutic appearance on our currency. Anyone intrigued enough to look can find it on the back of any one-dollar bill, where it apexes the pyramid on the reverse side of the Great Seal of the U.S.A.

Counting time is not so important as making time count. — James J. Walker

Book Reviews

If we encounter a man of rare intellect, we should ask him what books he reads.
— Emerson

THE FADING FAMILY PHYSICIAN — by Judge M. Lyle, M.D., Henry L. Geddie Co., $3.00 postpaid. Orders accepted at Book Dept., 510 S. Ballinger St. Fort Worth, Texas.

One man's experience as a general practitioner over a span of forty years has been incorporated into The Fading Family Physician, by Judge M. Lyle, M.D., just published by Henry L. Geddie Co., Fort Worth, Texas. Dr. Lyle recounts his experiences as a Mississippi farm boy and his early years in medical school, tells of the many things that can happen to a doctor engaged in general practice, and draws the conclusion that the modern type of family physician is giving way to the specialist.

"Many feel that the General Practitioner or the family doctor will fade out entirely except in the rural areas where one cannot easily reach the city or a hospital," Dr. Lyle writes. "Too, a lot of medical literature has been advocating that the medical internist become the family doctor. Some of the specialists think that the family doctor should be done completely away with in the cities and the diagnostician should fill his shoes."

"I feel that we must make the patient the central unit and co-ordinate everything for his good and well-being," Dr. Lyle writes.

Henry L. Geddie
Fort Worth, Texas

HOW DIABETICS CAN EAT WISELY — Dorothy Tompkins Revell. T. S Denison. Minneapolis. 1964, 172 pages.

Mrs. Revell is the dietitian for the Dakota Clinic in Fargo. She has written in this little book a handy kitchen aid for the diabetic or his cook. The new diabetic, saddened by the gastronomic insult of a diet list on a sheet or two, can turn gladly to such a book as this for relief from the monotony of a rigidly enforced diet. Mrs. Revell clearly indicates the wide choices that are available within the limits of a diabetic diet.

She recommends polyunsaturated fat, and many of her recipes for diabetic foods include such oil. As Kinsell puts it in his foreword: "It is still not possible for anyone to promise the diabetic who follows such a program that he will have major protection against the development of blood vessel disease, but it seems increasingly probable that this is so." The recipes, to this reviewer who knows his way about a kitchen, seem occasionally somewhat incompatibly compounded, as, for instance, green grapes halved served with canned salmon; or fresh apple and chicken salad. An occasional sentence loses its meaning in the shuffle of words: "Sometimes it is necessary to substitute and/or clear liquid foods for solid food."

Reuben Berman, M.D.
Minneapolis, Minnesota

CURRENT PRACTICE IN ORTHOPAEDIC SURGERY — Volume 2, 1964, Adams, $13.50.

The second volume of this series should appeal to the general surgeon as well as the orthopaedic surgeon. Five of the nine chapters deal with fractures, including a very interesting discussion on the management of acute vascular injuries of the extremities authored by Paul Gryska, R. Clement Darling, and Robert R. Linton.

It seems to this reviewer that the greatest advantage to this type of yearly publication over a formal text rewritten every four to five years is that the topics covered in each new issue can relate to recent advances in orthopaedics. The fourth chapter on vascular injury is a step in the right direction. The volume in general should be favorably received.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

MODERN TREATMENT — A bimonthly publication. $16.00 per year. Harper & Row, New York.

MODERN TREATMENT consists of a series of symposia dealing in an up-to-date fashion with problems that are of interest to every practicing physician. Among the forthcoming symposia are the topics of epilepsy, headache, menstrual disorders, arthritis, intestinal malabsorption and acid peptic disease. The subscriber to MODERN TREATMENT can look forward with pleasurable anticipation to these well documented paperback symposia.

Carl O. Rice, M.D.
Minneapolis, Minnesota

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1. Schleif, R.H.: J.A.PH.A., 46:179,1957 *U.S. Pat. No. 3,062,714

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Keep patients under close supervision and make periodic blood counts. Use cautiously in patients sensitive to pyrazoles, in patients with histories of peptic ulcer, and in conjunction with sulfa drugs, the sulfonylurea hypoglycemic agents, and insulin, the actions of which may be potentiated.

In mobilizing urate deposits, the drug may precipitate acute attacks of gout, urolithiasis, and renal colic, especially in the initial stages of therapy. Ensure adequate fluid intake and alkalinize the urine. With renal impairment, test renal function periodically.

Adverse Reactions
The most frequent are upper gastrointestinal disturbances. The drug may activate peptic ulcer. Rash occurs infrequently. Although not reported to date, blood dyscrasias are a possibility.

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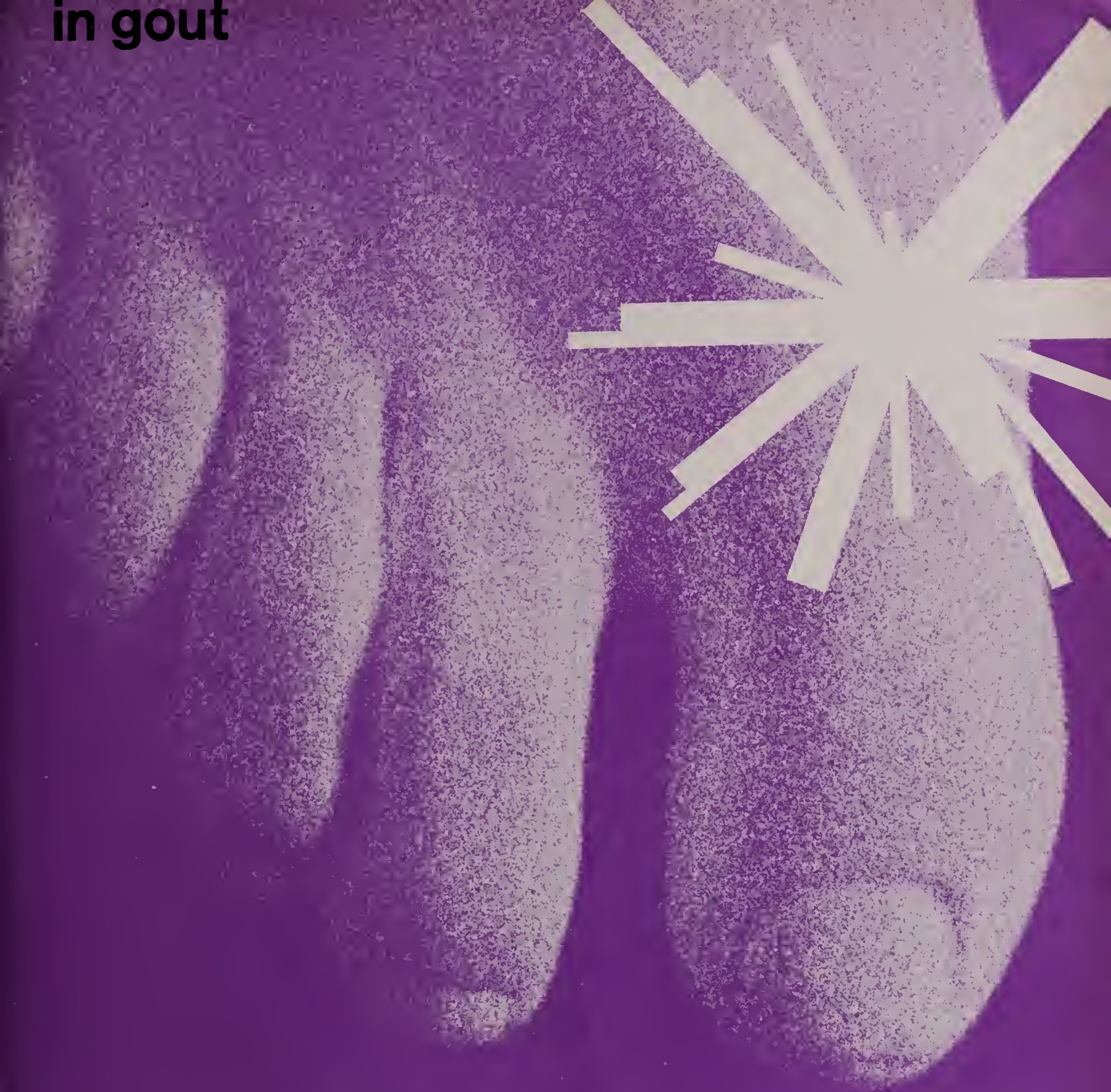
in gout



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Anturane, brand of sulfinpyrazone, materially reduces the number and severity of acute attacks of gout. It may also be used to counteract hyperuricemia induced by certain diuretics.

Because of its potency, the drug is often effective in patients refractory to other uricosuric agents. Patients can usually be maintained indefinitely on it without cumulative effects or development of tolerance.

Geigy

*Kuzell, W. C., et al.: Effect of sulfinpyrazone on serum uric acid in gout: a long-term study, Geriatrics

President's Letter Continued from Page 1271.

local societies should have such information in to the State Office by the middle of November. I would emphasize again that after the committees are appointed it is their duty and prerogative to become active in their sphere of interest.

In this issue of MINNESOTA MEDICINE the medical school and the profession of the State of South Dakota are being recognized. I am happy to see our editor give this attention to our good friends and neighbors of South Dakota, and we welcome their contributions to the pages of our journal.

JMStickney M.D.

J. M. Stickney, M.D.
President
Minnesota State Medical Association

For Pains in the Limbs

"For Pains in All the Limbs" the Scribe (of the Egyptian Papyrus) made a good start by instructing the Patient to mix up Castor Oil with Honey; but in the next few lines he spoilt everything by telling him to smear this all over the outside of his body instead of swallowing it and allowing it to do its work internally. Of course having got off the track at the start he found it impossible to right himself and accordingly went from bad to worse, his next effort being a poultice of Locusts which have been ground up in a mortar with Butter and Spices. For 'Pains in the Bones in Every Limb according to the Truth,' he recommended a poultice of Black Knife-stone with Fat, Honey, and Saltpetre as adjuvants. But according to the truth as we know it the use of Black Knife-stone, with or without Fat, Honey, and Saltpetre, in this connection is entirely fallacious, and not to be commended. The same can be said of the special poultice for the Thigh:

Bean-meal
Meal-of-the-pesen-bread
Sea-salt
Human Urine
Cook into one and apply as a Poultice.

And also for the Front-of-the-Shins, which was, however, let down more lightly:

The Inner-of-the-Shadfish; what is found in its Head
Soak in Honey and apply as a Poultice.

It Will Heal the Patient Forthwith.*

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*Bryan, Cyril: The Papyrus Ebers, D. Appleton and Company, New York, 1931, p. 60-61.

Modesty is a relative virtue; there is the modesty of a woman of 20, the woman of 30, the woman of 45. — Balzac

A writer often does his best work without being aware that he is doing it.
— Lea Rosten

Special Article

Regulatory Factors of Coronary Blood Flow

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THE STUDY OF the coronary circulation is actually a series of controversies, many of which have important clinical implications. Certainly the coronary vasculature functions under conditions much different from other systemic circuits. Many of the factors which regulate or modify the coronary hemodynamics are similar to those operative in all vascular beds. Others are apparently limited to the coronary system. Thus, in spite of the interest and the many investigations that have been carried out on the coronary vascular system, it still remains an enigma in many aspects.

Anatomic Position

Certainly not the least among the reasons for the situation mentioned above is the fact that the heart is approached only with some obvious disruption of its normal orientation in the closed chest cavity. This alteration is usually accepted by most investigators as being minimal insofar as the over-all responses studied are concerned. However, when an isolated heart is utilized, the preparation becomes more suspect. Nevertheless, much of the literature contains assumptions and evaluations of both physiologic and pharmacologic responses of the coronary system based on preparations much different than normal. Most of the more quantitative techniques for assaying coronary hemodynamics in situ by necessity require the presence of an anesthetic agent in the blood. This could conceivably be responsible for some alteration in the response patterns of the coronary vasculature. In all fairness it must be pointed out that the objections noted above could just as readily be applied to most vascular systems that are studied.

Sympathetic Nerve Activity and Drug Response

Probably one of the most controversial subjects of study has been the response of

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Continued

the coronary vessels to sympathetic nerve activation, and the presence of epinephrine and norepinephrine in the blood perfusing the vessels. In the author's opinion, another problem, namely that of the etiology of shock and its treatment, is very closely allied to the discussion of the functional activity of the coronary vessels. In most discussions of the vascular system and its response to various compounds related to the sympathetic neurohormones, and also to direct nerve stimulation, it is emphasized that the coronary and cerebral vessels are either qualitatively or quantitatively different from the rest of the body vasculature. The renal vasculature, at one time, enjoyed this distinction. First, let us examine the controversy of the differential sympathetic response of the coronary system and, secondarily, relate this to the problem of shock.

If the literature is examined it is at once obvious that not all investigators are of the opinion that the coronary vessels dilate in response to sympathetic nerve activation or to the presence of the catecholamines.[1-8] It should be kept in mind that many investigators utilize the fact that an over-all increase in coronary blood flow is obtained to indicate coronary dilation. It is just as conceivable to find an increase in blood flow per unit time through a constricted vasculature if the perfusing pressure is markedly raised. It has been the authors' experience that it is sometimes difficult to evaluate the response of vascular smooth muscle on the basis of the end result, namely blood-flow increase or decrease.[9-11]

Intra and Extravascular Factors

It is well recognized that a number of physical factors may, in varying degrees under varying conditions, influence the over-all coronary blood flow. The perfusion pressure is certainly of paramount importance.[12] Cross-sectional area of the vascular bed, as regulated by the arterioles, is another important determinant of both degree and direction, i.e., dilation or constriction, of response. The extravascular pressure exerts an influence on many vascular beds but is extremely important in the case of the coronary vessels.[13] This pressure is due primarily to the amount of extracellular and intracellular fluid in the myocardium at any particular time, and also to the basal "tone" of the heart muscle along with the contractile force or pressure exerted during each systolic phase of its activity cycle.

Autoregulation of Coronary Flow

A second regulatory mechanism of the coronary vasculature is the phenomenon of autoregulation. This is not a mechanism limited to the heart, as it apparently occurs in most of the vascular beds of the body. While the actual physical, biochemical, and physiological elements involved in the reaction are still controversial, it appears to be a means by which the relationship between flow and pressure are "sensed" by the very factors which create the phenomenon. The over-all purpose is to deliver the best available level of blood flow to the capillary beds for any given situation. Apparently the metabolic status and the degree of tension on the smooth muscle of the vessel walls are major determinants of this phenomenon.

Metabolic Modification

Intimately related to the concept of autoregulation are the effects of myocardial metabolism and the relation of the oxygen and carbon-dioxide tensions to this metabolic activity. Most studies indicate that hypoxemia induces an increase in coronary blood flow.[14] However, the mechanisms whereby this occurs are still being investigated. Some studies indicate that the effects of an increase in carbon dioxide and lactic acid on coronary blood flow are minimal. Nevertheless, both act on the coronary vasculature in the same manner as they do in other areas of the body, e.g., increase the blood flow.

Many other factors have been studied as to the role they play in the regulation of the blood flow through the coronary system. These include the adenine nucleotides, histamine, calcium and potassium ions, bradykinin, angiotensin, and many others. Most have failed to convince the investigators of their importance in the over-all regulatory scheme.

Arteriolar Activity and Response to Drugs

Certainly the factor that deserves the most consideration in the regulation of coronary blood flow are the peripheral resistance areas of the system, namely, the arterioles. The general consensus among investigators favors the opinion that under most physiological conditions this factor alone determines, in large part, the level of blood perfusing the myocardium. However, it is difficult to give this factor independence. In the author's opinion, it is somewhat analogous to the status of the pituitary gland some years ago. In present-day thinking it is often difficult to determine if this gland is the master or the slave. So it is with the arterioles, as many factors determine the degree of tension to be exerted by the component smooth muscle cells in the vessel walls.

Relationships of Blood Flow and Arteriolar and Drug Response to the Etiology and Treatment of Shock

As was mentioned previously, the relationship betwen the response of coronary vessels to sympathetic nerve stimulation or catecholamine presence in the perfusing blood and the etiology of shock are clouded by marked, and many times emotional, disagreements. Much of the previous history of the rationale for the treatment of the various classes or types of shock is based in large part on the administration of vasopressor (vasoconstrictor) compounds. This approach is based upon the assumption that the primary parameter to be followed and altered is blood pressure. The reasoning is that if the pressure can be raised, the blood flowing through a given tissue will also be increased. Unfortunately, a simple hemodynamic principle was overlooked. That is, if a given procedure raises blood pressure by acting on the smooth muscle of the peripheral resistance vessels (arterioles), these vessels will decrease their caliber and consequently decrease the blood flow through a given tissue or organ.

What is the alternative to the idea that the blood pressure must be raised to combat the syndrome known as shock? The obvious one: increase blood flow to the tissues and organs. As a corollary, we will have to face the fact that the blood pressure may even be allowed to decrease. Thus, it is better to perfuse the tissues with blood at a lowered pressure than to try to force more blood through tightly constricted arteriolar vessels with a high pressure. This then is the rationale in shock therapy for the use of compounds which either block the release of the catecholamines, or their action on the arteriolar smooth muscle, or the use of compounds which are in themselves smooth muscle relaxants.[15,16]

Now when we consider the coronary system, many investigators believe the coronary smooth muscle cells react differently than the rest of the vascular beds of the body. However, as previously mentioned, a small minority, including the author, believe that the evidence is inconclusive, if not altogether incorrect. Certainly the response of the coronary vessels to all other parameters and factors is much the same as the rest of the systemic vasculature. Thus, the coronary response to hypoxemia, various vasodilator and vasoconstrictor drugs (other than epinephrine and norepinephrine), reactive hyperemia, various hormones, etc. are all strikingly analogous to the general vascular response patterns. This latter statement does not mean to imply that we should use teleological reasoning to prove a point, but rather that we should at least consider the possibility, and investigate with open minds, the alternatives.

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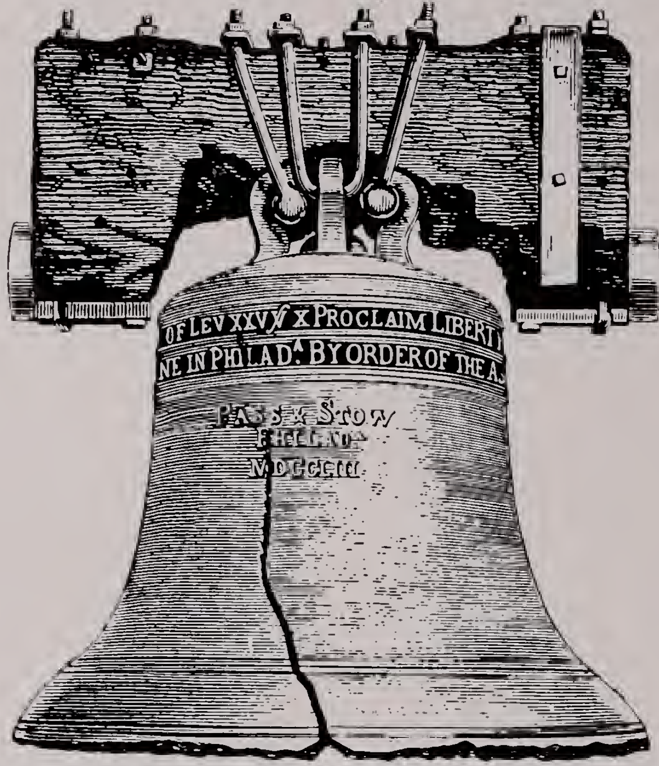
6-16 May be secured from the author or the reprints.

It is remarkable with what Christian fortitude and resignation we can bear the suffering of other folks. — Swift

19th CLINICAL CONVENTION OF THE AMA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Perinatal Mortality Study

Couvelaire Uterus

Case Report

The 33-year-old mother of this infant was Rh positive and had had four previous Cesarian section deliveries, with all four infants living and healthy. Her physician had planned to do a Cesarian section at 38½ weeks of gestation, but at 37 weeks the mother felt a pressure in the lower abdomen along with an urge to defecate. She fainted in the bathroom. When she regained consciousness, she telephoned and was rushed by ambulance to the hospital, where she continued to complain of increasing pressure and pain in the abdomen. She had had no external bleeding at home, nor was there any evidence in the hospital of external bleeding.

On admission the mother was in shock. Her blood pressure was 70/0, her hemoglobin 7.8 grams%. Her abdomen was very tender, and fetal heart tones were absent. The differential diagnoses included ruptured uterus or abruptio placentae. Couvelaire uterus was also considered. Blood transfusion was promptly started, and the mother was taken to surgery where a laparotomy revealed no tear in the uterus; but a Couvelaire uterus was present, dark blue in color. A low transverse Cesarian section was done, which showed the placenta completely separated with approximately 1000 cc. of clotted blood behind it. A dead infant weighing 5 lbs. 4 oz. was removed along with the entire uterus. The mother received 2000 cc. of blood and left the operating room in good condition.

An autopsy on the infant showed all of the organs to be normal for a stillborn of this size, except for small petechial hemorrhages scattered throughout all of the organs. These petechiae were interpreted to be on the basis of anoxia. Pathologic examination of the uterus showed it to measure 20 x 13 x 6.5 cm. The myometrium thinned, and there was hemorrhage into it.

Comment

Potter states; "A condition described as a Couvelaire uterus is occasionally associated with premature placental detachment. The wall of the uterus, especially in the lateral portions, becomes infiltrated by blood. Hemorrhage is present in muscle bundles, perivascular connective tissue and the subserosa, where it gives the uterus a deep purple color."

The Hennepin County Perinatal Mortality Study Committee presents this case as one that was well handled by the physician, who, presented with a case of sudden shock and abdominal pain in a pregnant woman, started blood promptly and did a laparotomy. It occasionally is necessary to do a hysterectomy with a Couvelaire uterus. The Committee will continue to study perinatal mortality, especially where it is associated with Cesarian section, erythroblastosis, or fetal death during labor.

Hennepin County Perinatal Mortality Study Committee.

Reference

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You go to your church and I'll go to mine, but we'll walk down the street together.
— Weirton Employes' Bulletin

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References: 1. Goldsmith, J. W.: Minn. Med. (Feb.) 1957. 2. Groskloss, H. H., Clancy, C. L., Healey, E. F., McCann, W. J., Maloney, F. D., Loritz, A. F.: Clinical Medicine (Sept.) 1955. 3. Codling, J. W., Lowden, R. J.: Northwest Med. (March) 1958. 4. Bethea, R. C.: International Record of Med. (May) 1960. 5. Lenz, W., Second International Conference on Congenital Malformations, N. Y., N. Y., (July) 1963.

Side effects: the incidence of drowsiness and other atropine-like effects is low. However, caution patients engaged in activities where alertness is mandatory.

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Robert Koch—Part II*

(1843-1910)

In 1882 Koch announced his discovery of the tubercle bacillus as the cause of tuberculosis. This was a great step forward in the understanding of the disease. Koch states in "The Aetiology of Tuberculosis" concerning the spread of this age-old scourge of mankind, "If the number of victims that a disease claims is the measure of its significance, then all diseases, particularly the most dreadful infectious diseases, such as bubonic plague, Asiatic cholera must rank far behind tuberculosis. Statistics teach that one-seventh of all human beings die of tuberculosis, and that if one considers only the productive middle age group, tuberculosis carries away one-third, and often more, of these." Koch's discovery ranks as one of the most important in the history of medicine. It was of great practical value in the diagnosis and control of the spread of the disease. By now the illustrious old Henle was indeed hailed as a prophet.

In 1890 Koch discovered tuberculin, a boiled glycerine extract from the cultures of tubercle bacilli growing in artificial media. Because of the specific reaction produced when tuberculin is injected into patients with tuberculosis, Koch made the tragic error of concluding that tuberculin was a cure for tuberculosis. Unfortunately many patients came to Berlin with the hopes of being cured. "As a therapeutic agent, tuberculin . . . failed to fulfill the expectation which Koch prematurely raised, but as a diagnostic aid it has proved of immense value."[4] "Tuberculin is of great value in diagnosis both in man and in animals. Thus it has been possible to test cattle and to collect herds of tested cows that are guaranteed to give milk free from all tubercle bacilli. In the United States, public health laws requiring periodical tuberculin tests of dairy herds have to a large extent eliminated the spread of tuberculosis from milk."[5]

Tuberculosis has long ceased to be the first cause of death in this country. Stimulated by Koch's discovery, our National Tuberculosis Association was founded in 1904. Today our state tuberculosis hospitals, state tuberculosis clinics, plus a vigilant year-round survey which includes tuberculin tests in schools and chest x-rays have brought about a steady decline in the disease. Tuberculosis patients who are discovered to have active disease are promptly admitted to one of the state tuberculosis hospitals for intensive treatment and supervision. Because of the effectiveness of modern antituberculosis drugs, the average duration of hospital treatment has been decreased to approximately ten months.

This is a great contrast to the middle of the 19th Century when the immortal musician, Frederic Chopin, was driven to the docks in a wheelbarrow by his indignant neighbors when they discovered he had tuberculosis.

Today many books and pamphlets on tuberculosis along with autographed letters of Robert Koch are part of a tuberculosis collection in the Welch Medical Library at Johns Hopkins.

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*See Minnesota Med 48:1241, 1965.

Continued

To Koch we owe also the beginnings of modern chemotherapy, important studies in antisepsis, both of which are organically related to the science of immunology. The Nobel Prize was awarded to Koch in 1905.

"Every nation owes an immeasurable debt to the man who gained victories over typhoid and rinderpest and sleeping sickness, uncovered the source of tuberculosis and cholera and Egyptian ophthalmia, and invaded continents, not for the conquest of his fellow-men, but to lead physicians in the warfare against pestilence and plague."[6]

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6. Robinson, p. 407.

History of Medicine in Wright County*

William B. Young, was listed in Monticello in 1893. He was a graduate of the University of Durham, Newcastle on Tyne, England in 1870. He is no longer listed in Monticello in 1896 and nothing more is known of him. He was not licensed in Minnesota.

Pioneer Dentists

Like many other rural areas in the state, Wright County had no resident dentist for a long time. There were only two before the 1890's — Drs. F. A. Atwater and S. C. Carter - who resided in Delano in 1880 and the early 1880's respectively.

The following list of pioneer dentists who came to Wright County on certain days or perhaps for a week each month makes no claims as to completeness. One of the earliest of these dentists was **Dr. C. Galpin,** who came for very short periods to Monticello around 1868, but may have come there as early as 1865. In 1866 **Dr. Patterson** of St. Paul may have come to Monticello for a week at a time. **Dr. A. L. Bausman,** of the firm Keith and Bausman, Minneapolis, came to Monticello as early as 1867 for a week or so at a time. The newspapers announced that one of the firm would come regularly. He came there at least through 1874.

Dr. J. H. Spalding of Hastings came to Rockford and later to Monticello from 1873 to at least 1876. The newspapers took note of the fact that he did not appear for a few months in 1876 — he had taken a course at the Ohio Dental College of Cincinnati and came home with a degree. He terminated his services to Wright County when he moved to Rochester, Minnesota, in September 1876 to form a partnership with Dr. J. M. Williams.

In 1875 and 76 **Dr. Avery** came to Delano on certain days. At first he saw patients at Young's Hotel and later at the Central House. He stayed in Delano only one or two days at a time. Early in 1879 (first notice appeared February 20, 1879) the **Woodburn Brothers** of Minneapolis announced they would make their services available in Delano the last week of every month. They used part of Dr. Rounsevell's office. For a considerable time it was **W. W. Woodburn** who made the trip to Delano.

John J. Catlin, M.D.
Buffalo, Minnesota
Robert Rosenthal, M.D.
St. Paul, Minnesota

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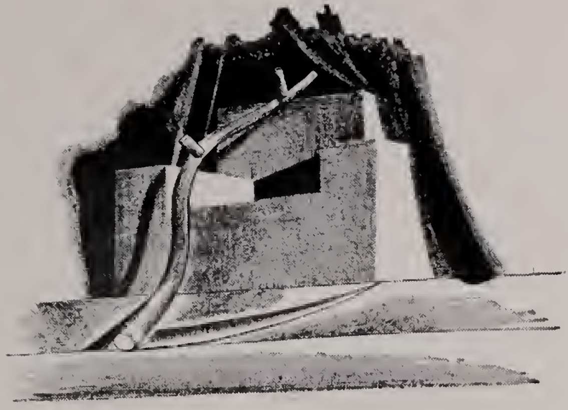
*See Minnesota Med 48:1242, 1965.



In Memoriam

He whom the gods love, dies young. — Menander

NORVIN R. SMITH, M.D.

Dr. Norvin Smith, 52, died July 7th, at his desk at the Hastings State Hospital. Dr. Smith was born in Big Springs, Nebraska, and graduated from the Nebraska College of Medicine in Omaha.

He was a member of the American Medical Association, Hennepin County Medical Society, and the Minnesota State Medical Association.

He is survived by his wife, a son and a daughter.

FRED Z. HAVENS, M.D.

Dr. Fred Havens, 85, a member of the Section of Plastic Surgery of the Mayo Clinic and emeritus professor of plastic surgery in the Mayo Graduate School of Medicine, died June 29, of coronary thrombosis. He was born in Hallville, Illinois, and graduated from the Rush Medical College of the University of Chicago.

Dr. Havens was certified as a specialist in otolaryngology and plastic surgery by the American Board of Otolaryngology and was a member of the American Academy of Ophthalmology and Otolaryngology, American Association of Oral and Plastic Surgery, American Laryngological, Rhinological and Otological Society, American Medical Association, American Laryngological Association, American Society of Plastic and Reconstructive Surgery, Minnesota Academy of Ophthalmology and Otolaryngology, Zumbro Valley Medical Society, Alumni Association of the Mayo Graduate School of Medicine, and a 50 Club and associate member of the Minnesota State Medical Association.

He is survived by a daughter and a son, Dr. Fred Z. Havens, Jr. of Riverside, California.

FREDERICK W. HOFFBAUER, M.D.

Dr. Frederick W. Hoffbauer, 64, chief of medicine at Hennepin County General Hospital, died of a heart attack July 30th. He was born in St. Paul and graduated from the University of Minnesota Medical School.

Dr. Hoffbauer was a professor of medicine in the University of Minnesota College of Medical Science. He was a member of the American Medical Association, Minnesota State Medical Association and Hennepin County Medical Association. Dr. Hoffbauer was a member of the Board of Editors of MINNESOTA MEDICINE.

He is survived by his wife.

WILLIAM R. BAGLEY, M.D.

Dr. William R. Bagley, 95, pioneer Duluth physician, died July 28th. He was born in St. Charles, Illinois, and graduated from the University of Michigan Medical School.

Dr. Bagley was one of the organizers of the Duluth Chapter of the Izaak Walton League and was president of the state society in 1934. Later he became a national director of the league. In 1940 he was chosen the 17th member of the Duluth Hall of Fame largely because of his community leadership.

He was a member of the American Medical Association and the St. Louis County Medical Society and a life and 50 Club member of the Minnesota State Medical Association. Dr. Bagley was a fellow of the American College of Surgeons.

He is survived by his wife, two sons and four daughters. Doctors Charles and Elizabeth Bagley of Duluth are among his survivors.

LEWIS S. JORDAN, M.D.

Dr. Lewis S. Jordan, 69, of Granite Falls, a past president of the Minnesota Tuberculosis and Health Association died July 17th. He was supervisor of the Riverside Tuberculosis Sanitarium in Granite Falls until its closing in 1963, and since then has been director of the Riverside out-patient department.

He was born in Alfred, New York, and graduated from the Eclectic Medical College in Cincinnati. He was a member of the American Medical Association, Camp Release District Medical Society and the Minnesota State Medical Association.

He is survived by his wife, Dr. Kathleen Jordan.

DAVID B. PETERSON, M.D.

Dr. David B. Peterson, 64, St. Paul physician, died suddenly July 21st. A graduate of the University of

Continued

Minnesota Medical School, Dr. Peterson had practiced medicine in St. Paul for thirty-five years. He was born in St. Paul and was a member of the staffs of St. John's and Bethesda Hospitals.

He was a member of the American Medical Association, Ramsey County Medical Society and the Minnesota State Medical Association.

He is survived by his two sisters.

MYRON LYSNE, M.D.

Dr. Myron Lysne, 60, Minneapolis physician, died August 15th, while boating near Fort Frances, Ontario. He was alone in his 14-foot skiff when he suffered a heart attack.

Dr. Lysne was born in Northfield and was a graduate of the University of Minnesota Medical School. He was a staff member at Fairview and North Memorial Hospitals, and a member of the Hennepin County Medical Society, Minnesota State Medical Association and American Medical Association.

He is survived by his wife, a son and a daughter.

MARIE A. MOQUIN, M.D.

Dr. Marie A. Moquin, 85, St. Paul physician, died June 26th. She was born in Oakland, California, and secured her medical degree from the Wisconsin College of Physicians and Surgeons.

Dr. Moquin was a member of the American Medical Association, Ramsey County Medical Society, and an associate member of the Minnesota State Medical Association.

JULIUS C. BUSCHER, M.D.

Dr. Julius C. Buscher, 74, St. Cloud physician, died August 8th. He was born in Osnabrueck, Germany, and obtained his medical degree at the University of Heidelberg-Kiel.

He was a member of the American Medical Association and Stearns-Benton Medical Society, and an associate member of the Minnesota State Medical Association. Dr. Buscher was the author of the book "The Doctor's Last Message."

He is survived by his wife and son.

MELVYN E. WITTHAUS, M.D.

Dr. Melvyn E. Witthaus, 38, White Bear Lake physician, drowned August 29th, when his sailboat capsized during a race on White Bear Lake. He was born in Kansas City, Missouri, and had been a resident in the St. Paul area about seventeen years. He was a graduate of Harding High School and the University of Minnesota Medical School.

Dr. Witthaus was a member of the American Medical Association, Minnesota State Medical Association and the Ramsey County Medical Society.

He is survived by his wife, two daughters and two sons.

JOHN A. MALMSTROM, M.D.

Dr. John A. Malmstrom, 63, East Range physician, died August 21st, 1965. He was born in Chisholm, Minnesota, and graduated from the University of Minnesota Medical School.

Dr. Malmstrom was a member of the American Medical Association, Range Medical Society and the Minnesota State Medical Association.

He is survived by his wife and two children.

ROBERT R. REMSBERG, M.D.

Dr. Robert R. Remsberg, 52, Tracy physician, died of a heart attack in his office, August 30th. He was born in Iola, Kansas, and received his medical degree at the University of Kansas.

Dr. Remsberg was a three-term member of Tracy's school board, the city's health officer since 1948, and was a Lyon County deputy coroner. He was a member of the American Medical Association, Lyon-Lincoln Medical Society and the Minnesota State Medical Association.

He is survived by his wife, two sons, and a daughter.

ARCHIBALD W. GRAHAM, M.D.

Dr. A. W. Graham, 87, Chisholm physician, died August 25, following a lingering illness. He was born in Fayetteville, North Carolina, and obtained his medical degree at the University of North Carolina and the University of Maryland. It was while Doctor Graham was in medical school that he gained notable reputation as a ball player. During the summers of 1905 and 1906 he played on the New York Giants' team as outfielder.

He came to Chisholm in 1909 and practiced there until his retirement. He was very active in many community projects, was a member of Kiwanis and the Masons, a member of the school board, a 50-club and associate member of the Minnesota State Medical Association, a member of the Range County Medical Society and the American Medical Association.

He is survived by his wife.

He that studies to know duty, and labors in all things to do it, will have two heavens — one of joy, peace and comfort on earth, and the other of glory and happiness beyond the grave. — Bowring

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The gods conceal from men the happiness of death, that they may endure life.

— Lucan

Medical Economics

No-Load Funds Versus Load Funds

A great deal of discussion and writing has been done on this subject in the past. With a few "no-load" funds starting to appear among the list of best performing investment funds, this load factor will require even more critical evaluation in the future.

In order to intelligently evaluate this "load" question, it is necessary to consider three basic loads or costs in connection with the acquisition, retention and disposition of investment fund shares.

(1) Acquisition Cost — "Front Load"

The majority of funds levy a charge for acquisition of their shares. This charge averages about 8% of net asset value. The funds that levy this charge do not usually charge a redemption fee upon disposition of their shares.

(2) Management Fee — "Middle Load"

This is the fee that a fund pays the managing company. It is an annual fee based upon a percentage of asset value ranging all the way from ¼% to 1½%. This management cost varies so widely that over a ten-year period, many "load" funds collect less fees (including acquisition charges) than the so-called "no-load" funds.

(3) Redemption Fee — "End Load"

This fee is almost standard among the "no loads," but very few "load" funds make a charge for redemption of shares. The most common charge is 1% of net asset value — a sizeable fee on a fund which has increased substantially in value over a period of years. The levying of this fee as a partial substitute for front load or acquisition charge tends to artificially improve the performance results of the "no loads."

If you combine all three of these "load" factors for a ten-year period, many of the so-called "no-load" funds are more costly to own than a "load" fund. To illustrate this principle, we have studied Massachusetts Investors Growth Stock Fund, a "load" fund, and DeVegh Mutual Fund, a "no-load" fund. We have assumed an initial investment of $10,000 on January 1, 1954, reinvestment of all distributions and liquidation of the shares on December 31, 1963.

The investment in Massachusetts Investors Growth Stock Fund incurred an $850 load upon acquisition and $633 management fees over the ten-year period for a total of $1,483, or 14.8% of the initial investment. The fund shares had a value of $41,836 on December 31, 1963, which would be the net liquidation value since there is no redemption fee for sale of shares.

The investment in DeVegh Mutual Fund was made without load charge, the ten-year management fee was about $1,380, and since DeVegh charges a redemption fee of 1% of net asset value, the redemption fee would be $415. Total fees on this "no-load" investment were 17.95% of the initial investment. The fund had a total value of $41,488 on December 31, 1963, less the $415 redemption fee, or a net value of $41,073.

This brief comparison illustrates the fallacy in looking at load or acquisition cost as a determining factor in choosing an investment fund. In this particular case, the total fees over the ten-year period of ownership were 3% higher on the "no-load" fund than they were on the fund charging 8½%.

It also illustrates the fallacy of choosing a fund even on the basis of total fees charged. On the basis of acquisition fee, you would choose DeVegh. On the basis of total fees, you would choose Massachusetts Investors Growth Stock Fund. This does not mean that DeVegh is an illogical commitment; on the basis of *net investment results*, it is still superior to 90% of the funds sold today. To eliminate it from consideration because of high over-all fees would be a mistake — just as the elimination of Massachusetts Investors Growth Stock Fund on the basis of its 8½% acquisition cost would be in very bad judgment.

We have maintained for years that "net investment result" is the only valid basis for the choice of funds. This comparison is just another means of strengthening this premise and illustrating the general irrelevance of fees charged. In choosing a fund, the amount invested and the net liquidation value of the shares at any given time are the most significant factors. In the event of equal investment quality of two funds, fees charged would be of possible significance — but even then total fees should be considered, not just the acquisition cost of the shares.

William D. Huntington*
Minneapolis, Minnesota

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*Northern Division Manager, Professional Management Midwest.

Early Specialization

The art of Medicine in Egypt is thus exercised: one physician is confined to the study and management of one disease; there are of course a great number who practice this art; some attend to the disorders of the eyes, others to those of the head, some take care of the teeth, others are conversant with all the diseases of the bowels; whilst many attend to the cure of maladies which are less conspicuous. — Herodotus (484-424 B.C.)

What is the single most important contribution to drug research?

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when President Washington signed the first U.S. patent law. For patents mean drug progress. For example, of the 604 important drugs introduced worldwide since 1941, the majority originated in the U.S. drug industry. By contrast, a major west European nation, which has no patent protection, contributed one.

How great is the contribution of drug patents? The answer is told in life itself: our children live 10 years longer than we, and need not suffer polio, measles, diphtheria, tuberculosis, rheumatic heart disease, and a dozen other illnesses we grew up fearing. We can expect these benefits to multiply—as long as our patent system remains strong.

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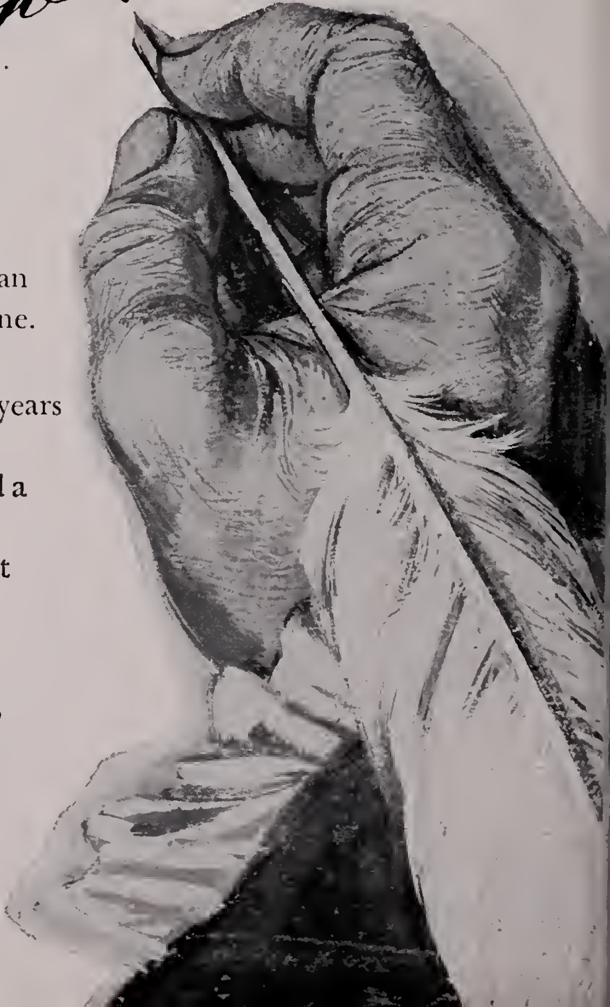

Meetings and Announcements

The joy of meeting not unmixed with pain — Longfellow.

OCTOBER

American Fracture Association Meeting, Las Vegas, Nevada on October 24-28. Contact: W. Compere Basom, M.D., 1220 N. Stanton St., El Paso, Texas 79902.

Annual Meeting of the Academy of Psychosomatic Medicine, October 11-13, Sherman House, Chicago. Edwin Dunlop, M.D., 150 Emory St., Attleboro, Mass. 02703.

51st Annual Clinical Congress of the American College of Surgeons, October 18-22, Atlantic City, New Jersey, Dennis and Shelburne Hotel. Contact: College.

Third Fall Meeting of the American College of Physicians, October 7-9, Deauville Hotel, Miami Beach, Florida. Contact: Edward Rosenow, Jr., M.D., 4200 Pine Street, Philadelphia, Pa.

Annual Otolaryngologic Assembly of 1965 will be held October 30 through November 5, in the new Illinois Eye and Ear Infirmary at the Medical Center, Chicago. Contact: University of Illinois, P.O. Box 6998, Chicago.

Annual Course in Postgraduate Gastroenterology of the American College of Gastroenterology, Americana Hotel in Bal Harbour, Florida, October 28, 29, 30. Contact: College, 33 West 60th Street, New York, N. Y. 10023

American College of Nutrition Annual Scientific Meeting, Americana Hotel in New York City, October 10th. Contact: R. A. Peterman, M.D., 3 Craig Court, Totowa Borough, New Jersey 07512.

American Academy of Pediatrics 34th Annual Meeting, October 23-28, Palmer House, Chicago. Write: Academy, 1801 Hinman Avenue, Evanston, Illinois.

American Association of Automotive Medicine Meeting, October 22-23, Mayo Clinic, Rochester. Write: Postgraduate Courses, Mayo Clinic, Rochester, Minnesota 55902.

NOVEMBER

Inaugural Scientific Program of the new Ancker Hospital, St. Paul, will be held November 11-13. Program will include two days of general medical meetings. Contact: James F. Hammarsten, M.D., Ancker Hospital, St. Paul.

Wisconsin Society of Pathologists Meeting, November 13-15, Pathology Department, Marquette University, School of Medicine, Milwaukee. Contact: Joseph L. Teresi, M.D. at 561 North 15th St., Milwaukee.

Annual Meeting of American Society for Colposcopy and Colpomicroscopy, New York City, Hotel Americana, November 6-7. Contact: Fritz Beller, M.D., New York University School of Medicine, 550 First Avenue, New York City.

Seventh National Conference on Medical Aspects of Sports, November 28-December 1, Philadelphia, Benjamin Franklin Hotel. Contact: Secretary, 535 North Dearborn Street, Chicago.

American Society of Cytology Meeting, Statler-Hilton Hotel, New York, New York, November 4-6. Contact: Warren Lang, M.D., 1012 Walnut Street, Philadelphia.

Committee on Injuries of the American Academy of Orthopaedic Surgeons will present a comprehensive postgraduate course on the Treatment of Injuries in Dallas, Texas, Marriott Motor Hotel, November 17-20. Contact: Sam Banks, M.D., 29 E. Madison Street, Chicago.

National Society for Crippled Children and Adults Convention, November 19-22, Palmer House, Chicago. Contact: Society, 2023 West Ogden Avenue, Chicago.

ANNOUNCEMENT

Hahnemann Medical College & Hospital, Philadelphia, postgraduate courses:

Nov. 22-24 — Symposium Cancer Chemotherapy, Sheraton Hotel.

* * *

Bush Leadership Fellows Program announced opening of competition for its 1965-66 awards, which will select four Minnesotans for 16 to 24 month fellowships. Sponsor of the program is The Bush Foundation of St. Paul. Deadline for receipt of applications is November 1, 1965. Applications can be obtained from David Roberts, W-3071 First National Bank Building, St. Paul.

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This authorizes your employer to make your savings automatic. He sets aside a small amount from your check each payday toward the purchase of U. S. Savings Bonds.

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Protection
For 25 Years

The Blue Shield

Blue Shield Celebrates Its 25th Anniversary

This year marks the 25th anniversary of the founding of the first Blue Shield type plan in 1939 by the California Medical Association.

The fledgling California infant in 1939 was the first step in a phenomenal quarter century of growth. Starting with the California plan, followed later in 1939 by a Blue Shield plan in Michigan, Blue Shield has grown to where it now comprises a network of 83 independent plans in the United States, Canada, and Jamaica, coordinated by the National Association of Blue Shield Plans in Chicago.

From barely 12 million subscribers in 1949, 10 years after its inception, membership in the succeeding 15 years has soared to over 53 million. Benefits paid to a record 53,450,349 Blue Shield subscribers in 1963 topped the billion dollar mark for the first time.

What are the reasons for such an outstanding growth record?

Coming out of the depression in the late '30s, Americans felt the need for a vehicle which would enable them to prepay their medical expenses. The financial ravages of the depression were disastrous to those who incurred heavy medical expenses.

The government was ready with a compulsory health insurance program when Blue Shield and other voluntary health care prepayment plans were made available to the people. Americans, given the opportunity to choose between government and voluntary health care, voted with their dollars for the voluntary approach in overwhelming numbers.

Today, more than 77 per cent of the United States population has some form of a voluntary health-care prepayment plan. Blue Shield covers 26.41 per cent of the United States population, handling 46 per cent of the medical and 36 per cent of the surgical coverage in this country.

The main reason for this widespread acceptance of Blue Shield is that benefits have kept pace with the medical-surgical needs of members.

Blue Shield strives to give subscribers "payment-in-full" for their medical-surgical expenses . . . and these payments are accepted as full payment by over 125,000 U. S. physicians.

Blue Shield has discovered that it can now extend benefits that it once thought impossible. Primarily, this is due to the unique relationship that Blue Shield has with both doctor and patient . . . and the nonprofit character of the organization.

At first, many Blue Shield plans limited coverage to inhospital surgical cases. A few included obstetrical cases and fewer offered limited coverage for nonsurgical cases. Almost all plans excluded coverage for diagnostic services.

Today, Blue Shield plans generally offer surgery in or out of the hospital, without limitation to the number of procedures; obstetrical services in or out of the hospital, including normal care of the newborn; and medical services in the hospital to 120 days or more.

Also usually offered is general anesthesia service in or out of the hospital by a physician anesthesiologist not employed by the hospital; diagnostic or therapeutic X rays; and professional laboratory interpretations in or out of the hospital.

Blue Shield, upon attaining the quarter century mark, has not paused to rest on its considerable laurels. It is moving ahead to new horizons of broader coverage for more people.

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Classified advertising rates are twenty (20) cents a word; minimum monthly charge $5.00; key number, fifty (50) cents additional.

Replies to advertisements with key numbers should be mailed in care of MINNESOTA MEDICINE, *496 Lowry Medical Arts Bldg., St. Paul, Minn. 55102*

SHARE SPACE AT SOUTHDALE? It might be the answer for you. Especially with new Fairview Hospital opening in October right next door. Medical specialist will share equipped and staffed suite. Contact: MINNESOTA MEDICINE — 325; 496 Lowry Medical Arts Building, St. Paul 55102.

BADLY NEEDED — G.P., Internist or Surgeon to associate with two-man G.P. partnership. Unapposed territory. New hospital, nursing home, children's home! Superb hunting, fishing, golf, pool, winter arena. Progressive town! Delmore Clinic, Roseau, Minnesota 56751.

A 13 MEMBER specialty group in the Midwest will need several men to replace and add to present staff. This has been a rewarding group for years, is now, and will be for years to come. We need 3 internists, 1 dermatologist, 1 ob-gyn, 1 pediatrician, 1 general and thoracic surgeon, 1 orthopedist, 1 ophthalmologist, 1 otorhinolaryngologist, and 1 psychiatrist. This is a very good town for a family man. Three colleges (1 a State College). Good schools and excellent recreation programs. Good hunting, fishing and water sports. Applicants should be board certified or completing requirements. Write MINNESOTA MEDICINE — 324; 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED PEDIATRICIANS AND INTERNISTS. Office space now available in new, modern, well established center — excellent opportunity for good earnings and professional pursuits — fastest growing suburban area. Write or phone A. G. Erickson, 7033 Edgewood Avenue North, Minneapolis Tel 533-7332.

WANTED: Board Certified or eligible internist to associate with group in large, active practice in Minneapolis. Group consists of Surgeon, Obstetrician, Pediatrician and Internist maintaining downtown and suburban offices. Partnership in mind. Contact: Jesse J. Barron, M.D., 1127 Medical Arts Building, Minneapolis, Minnesota 55402, FEderal 2-8259."

FOR RENT: Successful medical building. Opportunity for doctor to start new group. Rent at less than $3.00 square foot. Deluxe, modern, air-conditioned, all brick building with capacity up to four doctors. Located at 36th Avenue North and Noble Avenue in Northwest Suburban Minneapolis. For further information: Call Noble Drug at 588-9449 and ask for Ben or Lou.

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PROFESSIONAL AIR AMBULANCE. Multi or single engine aircraft. All weather and night flight capability, anywhere in the U. S. Oxygen, Respirator, Aspirator, Nursing service, all medications. Also full time M.D. Board Anesthesiologist providing all medical care in flight available on request. MIDWEST AIR TRANSPORTS, Operations Office, Municipal Airport, Waterloo, Iowa, Phone 319-2331083.

OFFICE SPACE now available in busy Bloomington. 713 square feet of new space in building with busy group of G.P.'s, dentist and suburban OB-GYN office. Ideal for ophthalmology, ENT or pediatrics. 8040 Penn Avenue South. 888-9211.

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WANTED INTERNIST, Board qualified or certified for 22-physician mixed group of general practitioners and specialists (East Range Clinic, Virginia, Minnesota). Salary first year, then full partnership. Centrally located in area of rapidly expanding economy.

WANTED: one or two general practitioners. Excellent clinic and hospital facilities. Rural practice established 18 years. Salary open, partnership if compatible. Lloyd H. Klefstad, M.D., Greenbush, Minnesota.

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A THREE MAN group needs a fourth general practitioner in a fast-growing West St. Paul area. Begin with salary and join partnership with full participating advantages. Write: MINNESOTA MEDICINE — 326, 496 Lowry Medical Arts Building, St. Paul 55102.

FOR SALE: Family practice in community just outside of Minneapolis. Ten minutes to 100 bed hospital. Full privileges assured. Finances no problem. Write: MINNESOTA MEDICINE — 327, 496 Lowry Medical Arts Building, St. Paul 55102.

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EXCELLENT PRACTICE AVAILABLE in downtown St. Paul. Attractive six room medical office practice, furniture and equipment available. Additional available space if desirable. Call Kenneth R. Larson, M.D. 222-6555 (office) or 225-7436 (home).

CHIEF OF PSYCHIATRIC SUPERVISORY STAFF needed to help with clinical supervision and teaching in expanding (18 resident physicians) fully approved residency training program. Ideal living in active community in the heart of Michigan's Water Winter Wonderland. Newly established position requires board certification in psychiatry and additional experience in clinical supervision. Salary range depending upon qualifications, $17,393 to $21,339. Unparalleled Michigan civil service benefits. Contact Arthur F. Dundon, M.D., Clinical Director, Traverse City State Hospital, Traverse City, Michigan. An equal opportunity employer.

GENERAL PRACTITIONER WANTED: to associate with physician-surgeon in Owatonna, a Southern Minnesota community, 25,000 population. Clinic building three years old; with five large treatment rooms, lab.; x ray; central supply; two doctors' offices; pharmacy; and business offices. Located next door to 85 bed city hospital. Good opportunity for partnership. Contact: O. W. Roberts, M.D.; 920 South Cedar Street; Owatonna, Minnesota. Phone 451-4630.

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A NEW, completely equipped two-doctor clinic in Southwestern Minnesota. New accredited 40-bed hospital. Large practice. Reasonable terms. Contact: Mrs. R. R. Remsburg, Tracy, Minnesota.

"...it is extremely difficult and sometimes impossible to differentiate between 'pure depression' and anxiety and it is questionable whether depression without a certain degree of anxiety really exists."

Lehmann, H. E., Canad. Psychiat. Assn. J. *4(S)*: 1-12, 1959

depression
anxiety
depression
anxiety
depression

An antidepressant designed for the clinical realities of office practice

As many physicians have reported, the large majority of neurotic depressed patients suffer from both depression and anxiety. It may be difficult to decide whether these patients are primarily depressed or primarily anxious. And yet drug treatment of only the symptom which seems more prominent may exacerbate the untreated element of the depression complex.

Consequently, it would seem that therapy specifically aimed at both the depression and associated anxiety and tension should increase success in treatment.

This is one of the important reasons why 'Deprol' has proved particularly helpful. For 'Deprol' acts rapidly both to lift the mood and to relieve the associated anxiety, tension and insomnia.

And side effects, at recommended dosage, have been infrequent and generally readily controlled.

Indications: 'Deprol' is useful in the management of depression, both acute (reactive) and chronic. It is particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination. It is also useful for management of depression and associated anxiety accompanying or related to organic illnesses.

Contraindications: Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

Precautions: *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

Benactyzine hydrochloride—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

Supplied: Light-pink, scored tablets, each containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.

Before prescribing, consult package circular. CD-5749

Deprol® meprobamate 400 mg. + benactyzine hydrochloride 1 mg.

WALLACE LABORATORIES / Cranbury, N.J.

too young
to be so tired...

revive interest...restore activity promptly with Alertonic®

Each 45 cc. (3 tablespoonfuls) contains: alcohol, 15%; pipradrol hydrochloride, 2 mg.; thiamine hydrochloride (vitamin B_1) (10 MDR*), 10 mg.; riboflavin (vitamin B_2) (4 MDR), 5 mg.; pyridoxine hydrochloride (vitamin B_6), 1 mg.; niacinamide (5 MDR), 50 mg.; choline†, 100 mg.; inositol†, 100 mg.; calcium glycerophosphate, 100 mg. (supplies 2% MDR for calcium and for phosphorus) and 1 mg. each of the following: cobalt (as chloride), manganese (as sulfate), magnesium (as acetate), zinc (as acetate), and molybdenum (as ammonium molybdate).

*Multiple of adult Minimum Daily Requirement supplied.
†The need for these substances in human nutrition has not been established.

the need for a tonic knows no age

Life *can* begin at forty—except when functional fatigue causes her to feel tired all the time; to start losing interest in friends and surroundings; to look and act older than her years. Alertonic—*a prescription tonic*—can help your patient become her normal self again. Alertonic helps relieve mild depression, revive interest and restore purposeful activity promptly...with a formula that is efficient *and* economical. Alertonic contains a mild central stimulant (pipradrol hydrochloride), 15% alcohol, essential vitamins and minerals. No hormones or MAO-inhibiting drugs are included. No iron. No iodine. One pleasant-tasting tablespoonful before each meal comprises the usual daily dose.

Indications: 1. Functional fatigue such as that often associated with: a depressing life experience or stressful time of life; advancing years; convalescence; limited activity or confinement. 2. Poor appetite and vitamin-mineral deficiency as they occur in: patients having faulty eating habits; geriatric patients who are losing interest in food; patients convalescing from debilitating illness or surgery.

Contraindications: As with other drugs with CNS-stimulating action, Alertonic is contraindicated in hyperactive, agitated or severely anxious patients and in chorea or obsessive-compulsive states.

Side Effects: Reports of overstimulation have been rare. Patients who are known to be unduly sensitive to the effects of stimulant drugs should be observed carefully in the initial stages of treatment.

Dosage: Adults, 1 tablespoonful; children (over 15 years old), 1 to 2 teaspoonfuls; children (4 to 15 years old), 1 teaspoonful. To be taken three times daily 30 minutes before meals.

THE WM. S. MERRELL COMPANY
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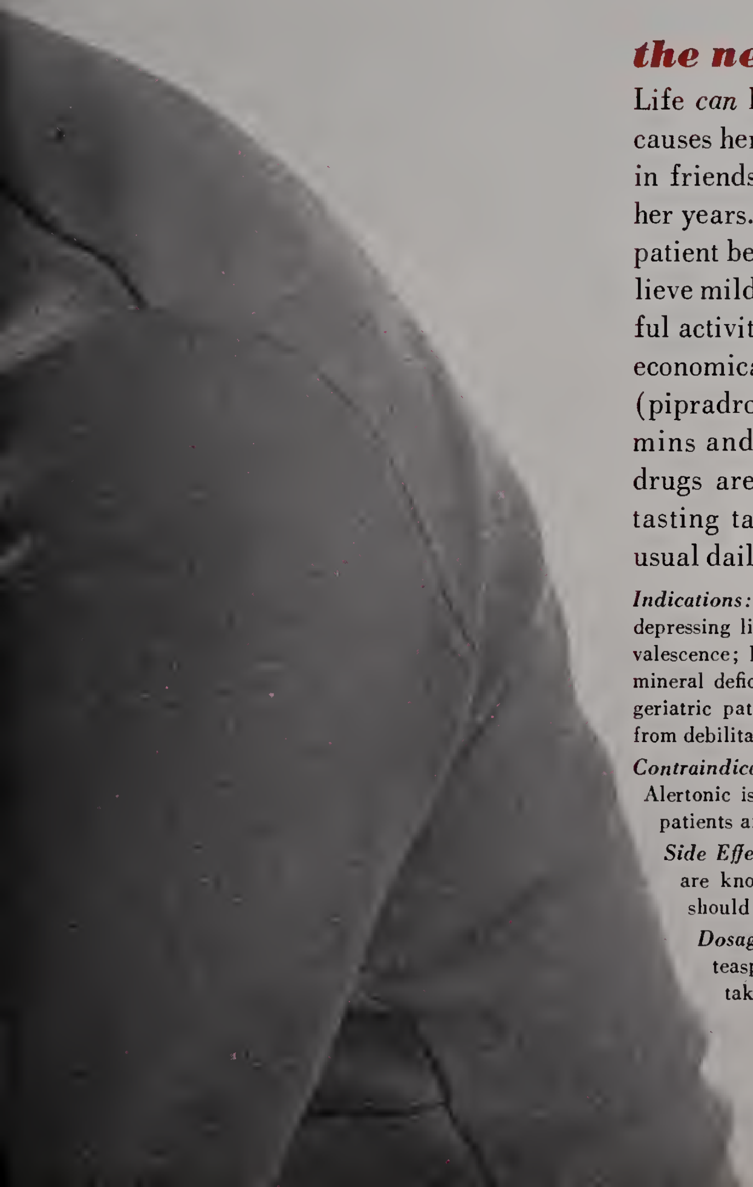

When uncontrolled diarrhea brings a call for help

When the diarrhea sufferer has run the gamut of home remedies without success, pleasant-tasting CREMOMYCIN can answer the call for help. It can be counted on to consolidate fluid stools, soothe intestinal inflammation, inhibit enteric pathogens, and detoxify putrefactive materials—usually within a few hours.

CREMOMYCIN combines the bacteriostatic agents, succinylsulfathiazole and neomycin, with the adsorbent and protective demulcents, kaolin and pectin, for comprehensive control of diarrhea.

Indications: Diarrhea. *Contraindications:* Kaolin: Withhold if diverticulosis is present or suspected. *Precautions:* Sulfonamide: Continued use requires supplementary administration of thiamine and vita-

your ℞ for
Cremomycin
can provide relief

min K. Neomycin: Patient should be observed for new infections due to bacteria or fungi. *Side Effects:* Sulfonamide: Sensitivity reactions may occur (e.g., skin rashes, anemia, polyneuritis, fever; agranulocytosis with a fatal outcome has been reported). Reduction of thiamine output in the feces and of vitamin K synthesis has been observed. Neomycin: Nausea, loose stools possible.

Before prescribing or administering, read product circular with package or available on request.

promptly relieves diarrheal distress

Cremomycin®

ANTIDIARRHEAL

Composition: Each 30 cc. contains neomycin sulfate 300 mg. (equivalent to 210 mg. of neomycin base), succinylsulfathiazole 3.0 Gm., colloidal kaolin 3.0 Gm., pectin 0.27 Gm.

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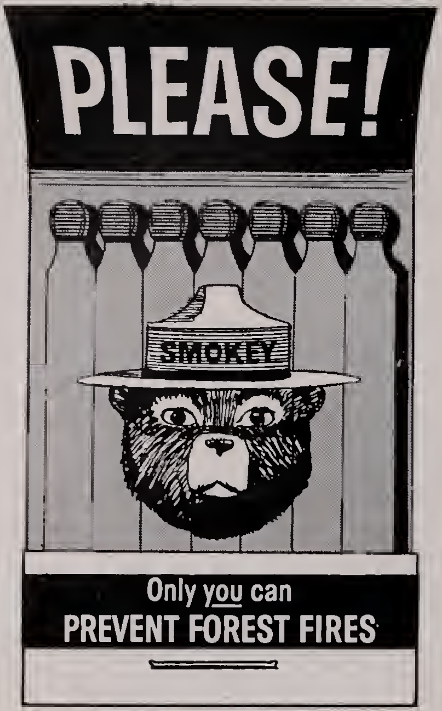

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brand of chlorthalidone

the long-acting diuretic

Indications
Many types of edema involving retention of salt and water.

Contraindications
Hypersensitivity, and most cases of severe renal or hepatic disease.

Precautions
Reduce dosage of concomitant antihypertensive agents by at least one-half. Discontinue if the BUN rises or liver dysfunction is aggravated. Electrolyte imbalance and potassium depletion may occur; take special care in cirrhosis or severe ischemic heart disease, and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended.

Side Effects
Constipation, dizziness, dysuria, headache, hyperglycemia, hyperuricemia, leukopenia, muscle cramps, nausea, purpura, thrombocytopenia, transient myopia, urticaria, vomiting and weakness.

Average Dosage
One tablet (100 mg.) daily with breakfast.

Availability
Tablets of 100 mg. in bottles of 100 and 1000.
For full details, see the complete prescribing information.

Geigy

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Division of
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How does Hygroton® brand of chlorthalidone stack up against other diuretics?

Not very high. In terms of one week's therapy, that is. The usual dosage is just one tablet per day. Very often, the dosage is even lower. So a week's therapy doesn't amount to much.

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For sheer diuretic effectiveness, choose Hygroton®, brand of chlorthalidone. It generally promotes more natruresis per tablet than the thiazides. We'll stack it up against any diuretic.

Geigy

Minnesota Medicine at a Glance

Heart Anatomy — Rinker Page 1273

Some of the anatomical features of the heart relative to normal and abnormal function are illustrated in this manuscript, and for an evaluation of the various heart disorders it is well to review this article and its illustrations.

Heart Sounds — Grissom Page 1279

Most of us think of only two heart sounds when we listen to the "lubb-dub" of the heart, but in reality there are many sounds. These sounds are made by the vibrations of the valves, the heart wall or the great vessels. If one is able to interpret each of the four heart sounds with the variations of each, one can obtain information much more meaningful than is evident from only a murmur. Some of the heart sounds are more evident in disease than they are in health and for that reason it is well to study in detail the four heart sounds as they have been so beautifully elicited by Dr. Grissom.

Ventricular Arrhythmias — Read Page 1284

Abnormal cardiac rhythms are divided into two broad categories, namely, a disturbance in the impulse conduction and a disturbance in the impulse formation. In this manuscript the arrhythmias arising as a result of an ectopic focus of impulse are principally dealt with. Calcium deficiency is known to favor an automatic impulse formation, and the cellular concentration of acetylcholine formed in the heart muscle may also have a direct bearing on the development of ectopic pacemaker in cardiac tissue. The cell membrane separates an extracellular fluid or high sodium and low potassium from an intracellular fluid of high potassium and low sodium. These ions are continuously diffusing into and out of the cell, and as they change, an electrical potential of 50 to 90 millivolts exists across the cell membrane to influence the myocardial activity. Ventricular arrhythmias are correlated with a large myocardial potassium loss. Substances which restrict the myocardial potassium loss may be effective in suppressing ventricular arrhythmia.

Cardiac Muscle — Scott Page 1292

With the electron microscope the myofibrillae, the filament, and the intercalated discs have been well illustrated. The variations in the structure from that of skeletal muscle are related to the fact that cardiac muscle fibers must contract frequently and simultaneously without long periods of recovery.

Electrolytes in Cardiac Disorders — Shaw Page 1297

The level of body fluids is regulated very closely by the balance between the fluid intake and the fluid output. The water and sodium content of the blood are under the regulatory control of vasopressin and Aldosterone. The rationale for the various types of heart failure are described.

The Chemistry of Heart Failure — Welty Page 1301

The common denominator of most forms of heart failure lies in the inability of the actomyosin system, which forms the myofibrils, to assimilate the energy of the phosphate bond and convert it into kinetic energy of contraction.

Heart failure can be divided biochemically and hemodynamically into the high output metabolic failure and low output nonmetabolic failure: the former represented by the cardiac failure of anemia, thyrotoxicosis, beri beri, etc. and the latter represented by low output congestive heart failure.

In observing the protein content of hypertrophied rat hearts it has been demonstrated that there is an increase in the myoglobulin and mitochondrial fractions. Associated with the stress factor of congestive heart failure there is an abnormal actomyosin and also an abnormality in the myosin complex.

The Myocardium and Drugs — Spencer Page 1305

The drugs used in myocardial disease can be divided essentially into three types: the myocardial stimulants which include the glycosides; the sympathomimetic amines, which also stimulate the myocardium but have a marked effect on other systems as well; and the myocardial depressant.

The cardiac glycosides are derived principally from digitalis, and though their action is principally on the heart muscle they are dependent upon calcium, potassium and other electrolytes within the body.

The sympathomimetic amines act principally upon the sympathetic nervous system. The chief disadvantage of these drugs is that the action is fleeting.

The myocardial depressant drugs act through their ability to inhibit the effects of intracellular potassium. They depress the vagus, the sinoauricular and atrioventricular nodes, and they inhibit the conduction through the bundle of His. They are indicated where depression of cardiac automaticity is desired.

Transaminase — Critz Page 1309

The determination of transaminase as an index of myocardial infarction was first described by La Due in 1954. It is suggested that the increase in the transaminase represents an attempt of the organism to convert an increased amount of amino acids into keto acids which in turn could enter the Krebs cycle and result in an elevated production of the adenosine triphosphate, thereby aiding the animal to meet the increased work load induced by the cardiac muscle. There are many conditions in which an elevated serum glutamic acid does not indicate myocardial damage; but with the clinical history of myocardial infarction, it would be rare to find a normal transaminase level.

Continued

Nutrition, Cholesterol and Heart Disease — Anderson Page 1314

A highly competitive middle-aged, slightly obese individual who is a sedentary heavy smoker with an elevated blood pressure and a serum cholesterol should have been alerted many years previous to his present condition that he would be a good bet to suffer some sort of cardiovascular accident if he did not change his living habits. Diet, along with the control of an elevated cholesterol, is only one of the many facets designed to aid in the diminution of cardiovascular disease. A philosophy of life must be developed to enable one to compete adequately with the stresses of the affluent society.

Thrombolytic Agents — Jewson Page 1363

The use of a thrombolytic agent for the purpose of lyseing a newly formed clot would appear to be a major advance in the therapy of thromboembolic cardiovascular disease. Because anticoagulants have very little benefit in restoring circulation to the ischemic area, it is postulated that the use of a thrombolytic agent might dissolve the clot and thereby provide better revascularization. The major disadvantage in the use of thrombolytic agents appears to be the formation of antibodies. Retreatment would then be especially difficult because of the increased amount of streptokynase that would have to be used to neutralize the antibodies and the hypersensitivity that might therewith develop.

Nonmetallic Implants — Nelson and Ivins Page 1371

This is a review of the various types of grafts, implants, and tissue substitutes which have been used primarily in the field of orthopedic surgery. The various criteria for the use of nonautogenous material are detailed, the principal obstacles to the use of exogenous material being antigenicity and rejection, foreign body reaction, loss of function, infection, and inadequate knowledge of the final fate of implants.

The processed heterologous bone graft, based on the work of Anderson et al., appears to offer a considerable number of advantages and can be commercially prepared.

The tissue substitutes, polyurethane, acrylic, tetrafluoroethylene, and the silicones offer interesting possibilities for the future.

Coronary Blood Flow — Geber Page 1387

For a provocative evaluation of the regulatory factors of coronary blood flow, this manuscript should be studied. The author points out that the evidence suggesting that the coronary smooth muscle cells react differently than the rest of the vascular beds of the body is inconclusive, if not altogether incorrect.

Physician's Diary

Let friendship creep gently to a height; if it rushes to it, it may soon run itself out of breath. — Fuller

Dr. N. N. Sonnesyn of LeSueur became chief of the medical staff at the Minnesota Valley Memorial Hospital at the hospital's staff meeting in June. **Dr. Dale Bergeron** former chief has accepted an appointment at the Marine Hospital in San Francisco, California.

* * *

Doctors Gerald J. Gleich, Carlo M. Veneziale, Richard O. Lundborg, Lillian R. Elveback, Sait Tarban, Jean Reiher, J. Paul Marcoux, Donald R. Krabill, James B. Bassingthwaighte and M. Robert Wilson, Jr. have been appointed to the staff of the Mayo Clinic, Rochester, as consultants.

* * *

Dr. R. C. Magnuson and family left August 18th for a three and a half months' trip to the Middle East. After a tour of the Holy Land, they will be spending three months at the Baptist Mission Hospital in Gendeberet, Ethiopia, with **Dr. Tom P. Coleman.**

* * *

Dr. William S. Eisenstadt of Minneapolis was recently elected to the Board of Regents of the American College of Allergists.

* * *

The citizens of Milan recently paid tribute to **Dr. M. A. Burns** who has practiced sixty-seven years in that town. Dr. Burns is ninety-one.

* * *

August 1st was the official retirement date of **Dr. L. H. Flancher** as superintendent and medical director of Sunnyrest Sanatorium, a career of more than fifty years connected with tuberculosis. Dr. and Mrs. Flancher will live in Detroit Lakes.

* * *

Dr. Edward O. Ferris, a Mayo Clinic surgeon, was elected president of the Mayo Graduate School of Medical Chapter of Sigma Xi at the society's annual meeting.

* * *

Dr. Don H. Spangler, a veterinarian from Atwater, was installed president of the American Veterinary Medical Association in July.

Dr. Maurice B. Visscher, distinguished service professor of physiology and head of the physiology department at the University of Minnesota, has been elected to a five-year term as president of the National Society for Medical Research.

* * *

Dr. Herman J. Moersch, emeritus head of a section of medicine in the Mayo Clinic, was awarded the gold medal of the American College of Chest Physicians for "meritorious service in diseases of the chest" at a session of the college in New York City.

* * *

NEW LOCATIONS: **Dr. Rodney C. Johnson** of Minneapolis has joined the staff of the Sheboygan, Wisconsin, Clinic . . . **Dr. T. J. Lelwica** is locating in Staples . . . **Dr. Jack Naros** has opened up an office at the Crosby Clinic . . . **Dr. Clifford A. Pesonen**, Aurora, will join the medical staff at the Austin Clinic . . . Doctors **Robert Cowger** and **Robert Hegrenes** are practicing at the River's Edge Medical Clinic in Farmington . . . **Dr. Donald S. Asp** has joined the Parkers Prairie Clinic in Parkers Prairie . . . **Dr. David G. Smith** has become an associate with **Dr. James W. Bratholdt** and **Dr. David R. Philip** of the Watertown Medical Clinic and **Dr. Cecil Leitch** has joined the Litchfield Clinic.

* * *

Dr. James C. Cain, consultant in medicine in the Mayo clinic, was named chairman of the National Advisory Committee on Selective Service by President Lyndon B. Johnson.

* * *

Dr. F. R. Kotchevar was guest of honor at a testimonial dinner in Eveleth recently. He is a staff member of the East Range Clinic.

* * *

Dr. Robert R. Kierland, head of the Section of Dermatology of the Mayo Clinic, has been elected an honorary foreign member of the Polish Association of Dermatology and an honorary member of the Portuguese Society of Dermatology and Venereology.

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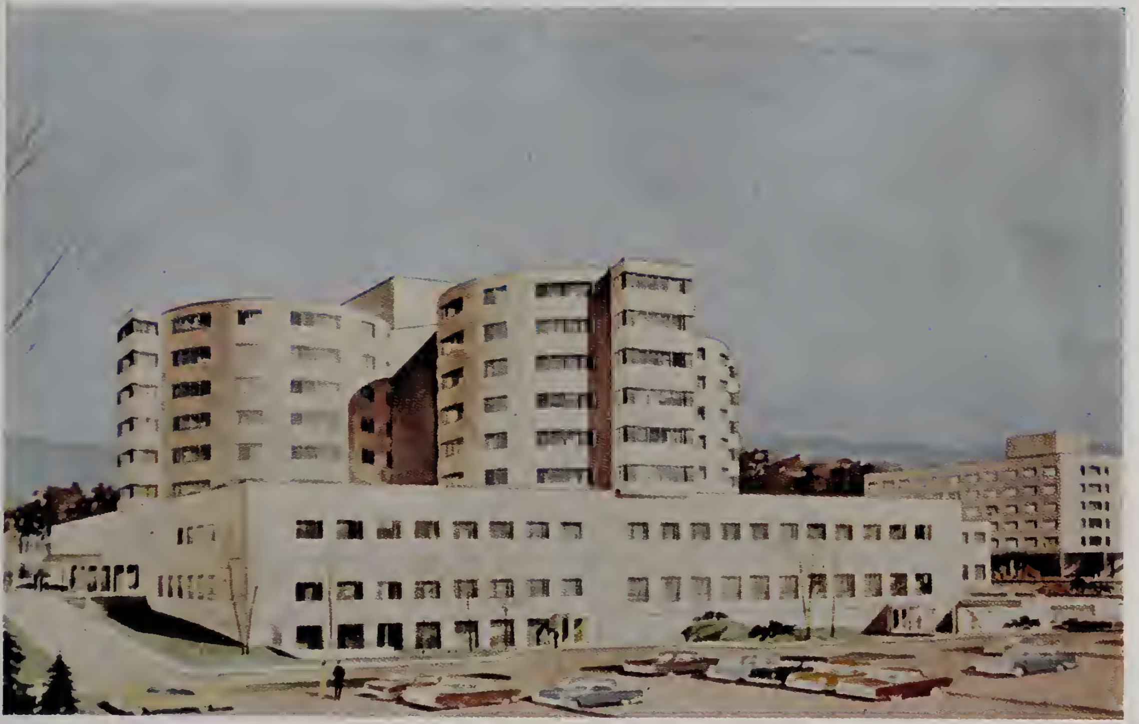

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vol. 48 #11

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(1) Portnoy, J.; Brewer, J. and Harris, A.: PUBLIC HEALTH REPORTS, *77:*645-652, August 1962. (2) Joseph, J. M. and Warner, G. S.: A WORKSHOP MANUAL, Md. State Dept. Health, Bureau of Lab., Balto., Md., September 1962. (3) Wollenweber, H. L.: OFF. PATH., *2*, February 5, 1963. (4) Portnoy, J.: MILIT. MED., *128:*414-417, May 1963. (5) Portnoy J.: THE AMER. JOUR. OF CLIN. PATH., *40:*473-479, November 1963. (6) Buck, A. A. and Mayer, H.: THE AMER. JOUR. OF HYG., *80:*85-90, July 1964. (7) Brown, W. J.; Donohue, J. F. and Price, E. V.: PUBLIC HEALTH REPORTS, *79:*496-500, June 1964. (8) Clayton, J. L.; Lindhardt, E. M. and Fraser, R. S.: PUBLIC HEALTH LAB., *22:*206-207, November 1964. (9) Lucatorto, F. M.; Katz, B. D. and Toto, P. D.: THE J.A.D.A., *69:*697-699, December 1964. (10) Portnoy, J.: PUBLIC HEALTH LAB., *23:*43, March 1965. (11) Reed, E. L.: PUBLIC HEALTH LAB., *23:*96-103, May 1965.

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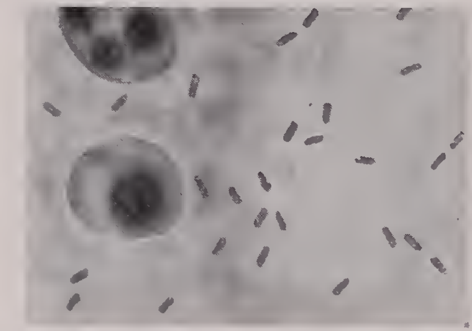

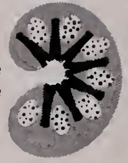

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President's Letter

In a few months Public Law No. 89-97 (Medicare) will be a fact of life which most of us did not ask for or think necessary. Whether we like it or not we cannot ignore it. Numerous conferences between administrative personnel of the Department of Health, Education, and Welfare and the medical profession have made it evident that government administrators are disposed to initiate Medicare with as little disturbance of the existing doctor-patient relationship as possible. Provisions are in the law which should result in the approval of almost all of the Minnesota hospitals which are presently licensed by the State Board of Health and there is nothing in the law which will prevent free choice of physician by the patient. The freedom of the physician to make his usual and customary charges and to look to the patient for payment to him is maintained, since the contract under Part B of Medicare is between the patient and the selected carrier unless the doctor elects to take an assignment of fees from the patient. Health, Education, and Welfare officials are emphatic that "reasonable fee" referred to in the law is to be interpreted as the usual and customary fee without regard to the patient's financial status. This will apply to those who at present may be charity patients and under a welfare fee schedule which is definitely below the usual and customary.

Utilization committees will be required in all participating hospitals and nursing homes. This concept is not new; in fact, many hospital staffs throughout the country are cooperating with such committees which have been formed voluntarily with the full approval of medical societies. The new law is broadly worded requiring only that there must be physician representation on Utilization Committees. Health, Education, and Welfare officials have also stated that they will endeavor to make certification for hospitalization and home care as simple as possible.

Most of the regulations incident to the new law as presently interpreted are not different in principle from those which the medical profession has accepted. The proportion of the population covered is, of course, more extensive than any heretofore encountered.

Those engaged in negotiation with governmental agencies about the details of this or any other law are traditionally suspicious that interpretation made at the inception will be more acceptable than that which may subsequently be deemed necessary. In my opinion it will be in the best interests of the practicing profession to cooperate fully with the present administration of Health, Education, and Welfare and the appointed carriers in order that we may have the maximum representation to maintain and strengthen the traditional freedoms of the physician in the application of Medicare. To do otherwise will give an advantage to those who do not fully represent the medical profession. Our opinions are being honestly solicited, and they should be thoughtfully given and diligently defended.

It is significantly appropriate that in this issue of MINNESOTA MEDICINE special recognition is being given to Ancker Hospital. The alumni of its training programs are numerous in this and the surrounding states. In offering our congratulations and best wishes to all those associated with Ancker Hospital, we know that the future is very bright.

JMStickney M.D.

J. M. Stickney, M.D.
President
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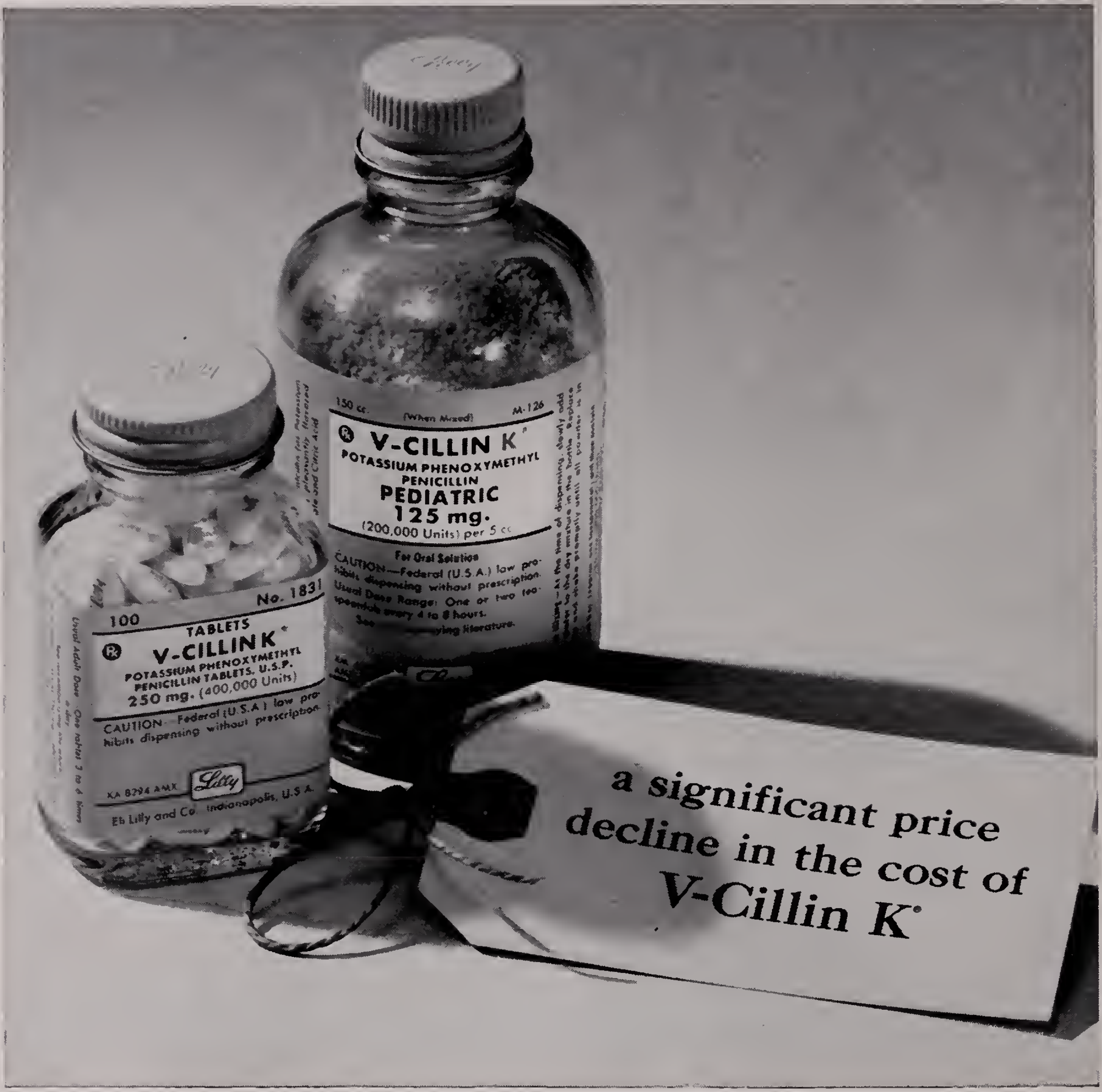
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Usual Dosage Range: 125 mg. (200,000 units) three times a day to 250 mg. every four hours.

Supplied: Tablets V-Cillin K, 125 or 250 mg., and V-Cillin K, Pediatric, 125 mg. per 5-cc. teaspoonful, in 40, 80, and 150-cc.-size packages.

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Use of Digitalis in Pediatric Patients

Essentials for the Practicing Physician

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IN THE PEDIATRIC age group, almost 90% of the patients who develop congestive heart failure are less than one year old.[1] The majority of these die in infancy.[2] In the first days and weeks of life, unsuspected severe congenital heart disease may suddenly manifest itself with respiratory distress and rapid progression of circulatory failure to death. An appreciable number of these infants have congenital heart lesions which are potentially correctable or can be alleviated by prompt surgery. Examples are coarctation of the aorta, aortic atresia and pulmonary atresia. The opportunity for successful treatment, however, rapidly adminishes with time, once cardiac distress has become apparent. Survival will be improved if special diagnostic procedures and emergency surgery can be carried out prior to exhaustion of the small energy reserves, depletion of catecholamines** and development of severe metabolic acidosis resulting from tissue hypoxia. The indication for emergency surgery is given in many instances (coarctation of the aorta, for example) if the response to digitalis treatment is unsatisfactory. Several critical, life-saving hours may, therefore, be gained if the first physician to examine the infant in distress, whether he be the obstetrician, general practitioner, pediatrician, resident, or intern on call, can initiate digitalization and other supportive therapy. Postponement of treatment is then avoided while arrangements are made for emergency transfer to a hospital with a Pediatric Cardiology Service.

The following data and discussion are designed to serve the practicing physician in his diagnostic and therapeutic considerations so that the delay encountered by the consultation of special literature will be minimal.

Diagnosis of Congestive Heart Failure

Congestive heart failure in infants is usually associated with an increased respiration rate (a rate above 55 per minute in the newborn at rest if counted over an entire minute) and with inspiratory retraction of the lower ribs anteriorly. Inspirations may become less labored due to exhaustion of the infant as heart failure progresses, while the respiration rate tends to remain in the range of 70 to 100 per minute or may increase further with ineffective ventilation. Rales are rarely found in infants except in the terminal phase of pulmonary edema.

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**See Test Your Word Score Page 1491.

The blood pressure tends to be low in circulatory failure. Excessive fatigue with feeding, vomiting, and failure to thrive may be the first signs of heart failure in infants if the onset is more gradual.

The Heart Sounds

A heart murmur may be absent or masked by respiratory noises in the presence of marked tachypnea. The heart sounds may or may not appear muffled; a diastolic gallop rhythm is almost diagnostic of myocardial failure. The heart rate is usually fast during rest (above 160 per minute in young infants with failure), but the normal range is wide. Definitely abnormal fast heart rates, above 200 and occasionally exceeding 300 per minute, may occur with paroxysmal supraventricular tachycardia in infants and result in heart failure. This condition should be suspected if the rate is regular and too fast to be counted by auscultation. The diagnosis of PAT is established electrocardiographically.

Cyanosis

Cyanosis may not be noticable initially but may develop as a result of (a) low cardiac output with circulatory stasis manifested by slow disappearance of a blanched ring from pressure of the stethoscope, (b) incomplete oxygenation of pulmonary venous blood in pulmonary congestion and edema (usually improving somewhat with oxygen treatment), or (c) in newborns a significant right to left shunt through the patent or reopened ductus arteriosus and the foramen ovale secondary to increased pulmonary vascular resistance in hypoxia and hypercarbia. Severe cyanosis may be present without heart failure in intracardiac defects producing a shunt of venous blood into the arterial circulation, as in tetralogy of Fallot, or it may be associated with a failing heart in emergency conditions of the newborn as in atresia of the pulmonary valve with normal aortic root.

Enlarged Liver

The most sensitive index of cardiac failure in the infant is enlargement of the liver,[3] i.e., if the liver in newborns is palpable more than 3 cm. below the right costal margin when measured in the medioclavicular line, has lost its sharp edge, and is tender particularly when engorgement is acute. Emphysema of the lung with low position of the diaphragm may result in an erroneous impression of liver enlargement. Chest x-rays are helpful in recognizing this condition.

Peripheral edema is often manifested by a "puffy face" and a lustrous or shining appearance of the skin. Pitting edema is rare in infants. Systemic venous engorgement is a valuable sign in older children.

Heart Size

The heart size is clinically often difficult to evaluate in infants. X-ray evidence of heart enlargement is generally present in cardiac failure. Exceptions include congenital stenosis of the pulmonary veins, cor triatriatum, atresia of the common pulmonary vein with total anomalous pulmonary venous connection and other obstructive lesions at or above the mitral valve, all of which lead to engorgement of the pulmonary veins and may be responsible for circulatory failure in infancy. A reticular or granular appearance of the lung fields associated with normal heart size is a characteristic finding in this entity. If x-ray films are less than ideal, pulmonary congestion and edema are sometimes difficult to differentiate from pneumonia or increased vascularity due to an intracardiac left to right shunt. Since pneumonia and heart failure may concur, in clinically doubtful cases a therapeutic trial of digitalization in connection with antibiotic treatment is justified. The heart size in newborns may not be significantly increased at the onset of cardiac distress, but marked dilatation may develop within a few hours. Portable films taken at less than five to six feet or the presence of a large thymus gland can lead to overdiagnosis of cardiac enlargement, while the cardiac size may be underestimated in the presence of pulmonary emphysema, usually present in cyanotic congenital heart disease.

Therapy of Heart Failure

Supportive medical therapy[4]

Positioning in a semi-upright infant seat in a tent or isolette with humidified oxygen for relief of dyspnea and cyanosis.

Morphine in a dosage of 0.1 mg. (to 0.2 mg.) per kg. body weight in very restless infants with pulmonary edema[4] to prevent exhaustion due to excessive restlessness.

Mercurial diuretics: (a) meralluride sodium injection (mercuhydrin sodium) available in ampules and vials: each ml. contains 39 mg. mercury and 48 mg. theophylline; or (b) mercaptomerin sodium (thiomerin sodium) available in vials, solution and dry form (1.4 and 4.2 gm.): each ml. contains 40 mg. mercury. The dosage of either drug for infants in the first few months is 0.1 ml. I.M.; for older infants 0.20 to 0.25 ml., and beyond infancy up to 0.5 ml. I.M. This dosage should be given only once daily and not for more than two or three days. Increased loss of potassium in the urine must be expected; therefore great caution is required to prevent digitalis intoxication due to hypokalemia. Diuretics are useful in emergency treatment of pulmonary edema. If the onset of cardiac failure is more gradual, it is preferable to defer mercurials to reduce the risk of digitoxicity during digitalization.

Restriction of sodium intake in the infant by using Lonalac formula (Mead Johnson). The prepared formula contains 1.1 mEq. of sodium per liter. After the initial beneficial sodium depleting effect, this formula may produce a low sodium syndrome if continued over long periods. If edema is relieved, it should be replaced by Similac 60/40 or SMA 26 (Ross Laboratories or Wyeth Laboratories respectively). Both of these formulas contain sodium in physiological amounts (6.5-7 mEq/L.) corresponding to breast milk. They are, therefore, safer than other formulas with higher sodium contents (Similac 11.2 mEq/L., evaporated milk in 1:1 dilution 16.9 mEq/L., whole cow's milk 16.9 mEq/L.). Frequent oral suctioning — if secretions are present — is indicated to prevent additional respiratory embarrassment. Gavage feeding in severe distress will preserve the infant's energy.

Digitalis

Digitalis is the most important drug in the treatment of failure in infants. It is recommended, although not equally effective, in all forms of heart failure. Probably the only contraindication is digitoxicity.[4]

TABLE I
Dosage of Digoxin (Lanoxin) for Infants and Children

		Total Digitalizing Dose*		
Age	Method of Administration	mg./kg.	per M^2 Body Surface Area	Total Daily Maintenance Dose**
Newborn (under 2 wk.) and premature infants	Intravenous or Intramuscular	0.03-0.05	0.6-0.75 mg.	1/10-1/5 of total digitalizing dose
Infants under 2 yr. (after newborn period)	Oral	0.06-0.08	1.5 mg.	1/5-1/3 of total digitalizing dose
	Intravenous or Intramuscular	0.04-0.06		1/10-1/5 of total digitalizing dose
Children over 2 yrs.	Oral	0.04-0.06	1.5 mg.	1/5-1/3 of total digitalizing dose
	Intravenous or Intramuscular	0.02-0.04		1/5 of total digitalizing dose

*Recommended method of administration with consideration of individual variation: 1/2 total dose at once followed by 1/4 total dose in 6-8 hours, and 1/4 total dose in another 6-8 hours, with maintenance therapy instituted 12 hours thereafter.

**Divided in 2 equal parts and given at 12-hour intervals.

CAUTION: Patient should not have had digitalis or derivatives for 2 weeks or more.

Digitalization is considered a therapeutic bedside experiment. The smallest effective dose is the safest and must be determined by close clinical observation and judgment of the effect. Tables serve to calculate the range within which most likely effective digitalization is possible (Table 1, Reference 5). Toxic effects may occur within this range if hepatic or renal function is decreased, and if electrolyte abnormalities, especially low potassium blood levels, are present or develop during treatment with diuretics or parenteral fluid therapy. Calcium given intravenously enhances digitalis effect and may precipitate toxicity.

'Lanoxin' brand digoxin is the preferred drug in pediatrics for a number of reasons. It is commercially available for parenteral and oral administration in concentrations suitable for infant dosages without further dilution (Table 2). The maximal effect is obtained rapidly: on intravenous administration in two to three hours, on oral or intramuscular administration in three to four hours. The excretion is so rapid that slightly toxic effects disappear usually within one day, and maximal duration of toxicity is unlikely to exceed two days. Most of the drug is excreted within 48 to 72 hours.[4] In order to maintain stable digitalization, however, the maintenance dose must be given in at least two divided parts at intervals of 12 hours.

TABLE 2
Recommended Technique of Digitalis Administration in Pediatric Patients

A. Lanoxin brand Digoxin Injection (Burroughs Wellcome) for intramuscular or intravenous use is available in 2 cc. ampules each containing 0.5 mg. (0.25 mg. per cc.)
CAUTION: Do not confuse with Digitoxin!
A standard glass tuberculin syringe with divisions of 0.01 cc. should be used if dosages for infants are to be measured. Disposable plastic syringes are less accurate and not recommended for this purpose.
The needle used for the injection should be filled with Lanoxin when the amount is measured so that the exact dose is delivered by injection.
The cc. scale of the syringe should always be used for measurement. Estimations on the minim scale are inaccurate and have resulted in errors and overdosage.
Before injection the nurse should check with the physician to exclude errors in measurement of the calculated amount.
The following conversion table may be helpful for the measurement of infant dosages:

1.0 cc. = 0.25 mg. Lanoxin Injection
0.5 cc. = 0.125 mg. Lanoxin Injection
0.4 cc. = 0.1 mg. Lanoxin Injection
0.2 cc. = 0.05 mg. Lanoxin Injection
0.1 cc. = 0.025 mg. Lanoxin Injection
0.05 cc. = 0.0125 mg. Lanoxin Injection
0.04 cc. = 0.01 mg. Lanoxin Injection
0.03 cc. = 0.0075 mg. Lanoxin Injection
0.02 cc. = 0.005 mg. Lanoxin Injection
0.01 cc. = 0.0025 mg. Lanoxin Injection

B. "Lanoxin" brand Digoxin Elixir Pediatric (Burroughs Wellcome) for oral use is available in bottles of 2 fl. oz. equipped with calibrated dropper. Each cc. of oral Lanoxin contains 0.05 mg. Note the difference in concentration between the oral and parenteral preparation! See Table 1 in regard to the differences in oral and parenteral dosages.

Administration of Digitalis

The intramuscular route, and, in emergencies, the intravenous route is used to initiate digitalis therapy in infants and small children to avoid uncertainty of absorption associated with vomiting and spitting up.

The range of the total digitalizing dose should be calculated on the progress sheet of the chart according to the digitalization schedule (Table 1). In order to prevent fatal errors in decimal points, the dose should be recalculated independently by another physician or a nurse. For technical details see Table 2.

Example

A two-day-old newborn of 3000 gm. body weight would require a total dose of Lanoxin for parenteral digitalization between 0.09 mg. and 0.15 mg., which corresponds to 0.36 cc. and 0.6 cc. (Table 2). A dose near the lower range is then tentatively selected so that it can be divided and measured accurately, for example, 0.10 mg. Lanoxin = 0.4 cc. The initial dose equal to ½ of total is 0.05 mg. contained in 0.2 cc. and is given at once intramuscularly or intravenously. The second dose equal to ¼ of total is 0.025 mg. in 0.1 cc. and is given four to eight (usually six) hours after the first dose intramuscularly. The third dose equal to ¼ of total is 0.025 mg. in 0.1 cc. and is given four to eight (usually six) hours following the second dose intramuscularly.

The apical pulse is checked at hourly intervals by an experienced nurse for any evidence of irregularity, bradycardia or tachycardia. Abnormal findings are immediately reported to the physician. An electrocardiogram is taken whenever any arrhythmia is suspected and routinely between the second and third dose. The infant is re-evaluated by the physician for any signs of toxicity before the second and third doses are given. If the desired effect has not been obtained four to eight hours after the previously calculated total dose has been given and no signs of toxicity are present, another quarter of the digitalization dose may then be given. This would increase the total dose required for digitalization to 0.125 mg., which is still below the upper range calculated initially for this infant. If this dose is effective, and no toxic signs are present, intramuscular maintenance therapy is begun 12 hours later.

The total daily maintenance dose for this infant is calculated on the basis of the actual digitalization dose of 0.125 mg. according to Table 1. The range is 0.0125 mg. (=0.05 cc.) to 0.025 mg. (=0.1 cc.). An average dose would be 0.01875 mg. (=0.075 cc.). Since volumes of less than 0.01 cc. cannot be measured with a tuberculin syringe, the dosage must be adjusted to a practical figure, for example, 0.02 mg. (=0.08 cc.). The total maintenance dose is then divided into two equal parts of 0.01 mg. (=0.04 cc.) of Lanoxin and injected intramuscularly every 12 hours to maintain stable digitalization. Further adjustments must be made according to the individual needs and as weight and age increase. In infants beyond the newborn period who do not spit up, and in older children, maintenance therapy is usually carried out with oral Lanoxin. Note the difference in oral dosage (Table 1) and in concentration of Lanoxin in the elixir for oral use (Table 2).

A favorable response to digitalization is associated with relief of dyspnea, improvement of tachypnea and tachycardia, recession of hepatomegaly, relief of edema, improvement of color and of food intake.

Digitalis Toxicity

While the electrocardiogram is not helpful to determine therapeutic efficacy of digitalis, it is an important aid in the recognition of toxicity. Almost any arrhythmia can be produced, including atrioventricular dissociation, atrial and ventricular premature beats, intra-atrial atrioventricular and bundle branch block, nodal tachycardia, atrial flutter and fibrillation, and ventricular tachycardia and fibrillation.

The infant may show an unusual lethargy, vomiting, diarrhea, abdominal pain and lack of appetite. Mild degrees of intoxication may develop as the result of slow accumulation during maintenance therapy and usually are easily treated by withdrawal of the drug and oral administration of potassium in the form of orange juice. After elimination of all signs of toxicity maintenance with a lower dose is resumed. Severe intoxication is almost always due to errors in dosage, confusion of glycosides with similar names, or accidental poisoning with tablets kept unlocked at home.

Treatment

Prevention of digitalis intoxication requires great care. The treatment of a serious toxic arrhythmia keeps one or more physicians at the bedside for many hours. In such instances, the following are recommended:[6]

A written order to stop the digitalis.

If kidney function is adequate, the electrocardiogram shows no evidence of hyperkalemia and no vomiting is present, oral potassium therapy with potassium triplex (15 mEq. of potassium per teaspoon), 1 teaspoonful three times daily or potassium gluconate (Kaon elixir) (20 mEq. of potassium per tablespoonful,) 2 tablespoonfuls daily.

If oral medication is impossible or ineffective, intravenous potassium administration may be considered. Continuous electrocardiographic monitoring and bedside interpretation by an experienced electrocardiographer are necessary. The solution should contain no more than 40 mEq. of potassium chloride in 500 cc. of dextrose (5% in water) and the total dose should not exceed 2 mEq. per kg. body weight (1 mEq. per pound). Administration must be very cautious to avoid potassium intoxication. The maximum dose for a 3-kg. infant would be 6 mEq. which equals 75 cc. of above solution. The infusion is started in a slow intravenous drip and is stopped if the arrhythmia disappears or peaking of the T wave occurs.

Potassium is not indicated in complete heart block since it may depress the atrioventricular node and ventricular conduction and may cause asystole. Instead isoproterenol (Isuprel) may be tried in 0.1 mg. doses intravenously.

Depression of the ionization of calcium may effectively reduce digitoxicity, since a synergistic action exists between calcium ion and digitalis.

Ethylenediamine tetra-acetic acid has been found hazardous because of severe hypotension, damage of proximal renal tubular cells, and other side effects.[7] It has recently been suggested to use sodium citrate in 4% solution or acid-citrate-dextrose solution (Baxter) intravenously as a chelating agent.[7] Our experience with this treatment is limited to one infant in which no untoward reactions occurred. The solution was given cautiously intravenously over four to five hours as indicated by the electrocardiographic findings. An anesthesiologist was in attendance to maintain a clear airway and respiration if this should become necessary. One should be aware of the hazard of tetany during this treatment.

Adequate treatment of the infant with cardiac problems is a challenge to everybody concerned with his care.

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WHAT'S YOUR DIAGNOSIS?

A white female, aged 46, gave a history resembling biliary colic. A cholecystogram revealed a nonfunctioning gallbladder, but there was a ring-like area of calcification 12 millimeters in diameter having the characteristics of a partially calcified gallstone (Figure 1). She was operated upon in January 1952, when the gallbladder was found to be thickened but no stone identified. The gallbladder was then removed. Postoperative convalescence was satisfactory.

She was then well until January 1954 when she developed nausea and right upper quadrant pain and, on occasions, had episodes of fever, bloating, intolerance to cabbage, apples, and a few other foods. These intermittent symptoms persisted, and in August 1957 an intravenous cholangiogram revealed "gallbladder filled with opaque material and multiple noncalcified stones." At this time she was again operated. The common duct was explored and also the liver up to the bifurcation of the right and left hepatic ducts, on the basis that there might be a intrahepatic second gallbladder. None was found. She had satisfactory healing but persisted in having intermittent bouts of fever and pain in the right hypochondrium. Six months after the second operation she was explored again. What is your diagnosis? Turn to page 1457.

Fireplace

What is more cheerful, now, in the fall of the year, than an open woodfire? Do you hear those little chirps and twitters coming out of that piece of applewood? Those are the ghosts of the robins and bluebirds that sang upon the bough when it was in blossom last spring. In summer whole flocks of them come fluttering about the fruit trees under the window; so I have singing birds all the year round. — Thomas Bailey Aldrich

Gardner's Syndrome

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FAMILIAL POLYPOSIS of the colon, associated with hard and soft superficial tumors such as exostoses, osteomas, fibromas, and desmoid** tumors, has come to be known as Gardner's syndrome.[1] It is inherited as an autosomal dominant characteristic. Because of the high incidence of carcinoma,[2] early recognition and therapy is important, as one half of these patients have carcinoma by the time they are 30 years old. We have recently encountered a young woman at Ancker Hospital who serves as a reminder that we should be alert to lesions which predispose to carcinoma.

Case Report

The patient is a 29-year-old white female who first noted a nodular growth in her abdomen during her first pregnancy at age 22. This was excised and found histologically to be a desmoid tumor (Figure 1). During the next six years she had numerous recurrences and excisions, one such recurrent growth causing obstruction of her right ileofemoral artery. A teflon prosthesis was used to restore circulation to her right leg. In an attempt to excise the tumors completely the anterior abdominal wall was replaced with teflon mesh. As this was unsuccessful, a course of radiotherapy was given, using Cobalt 60, with the left upper quadrant receiving 5150 rads over a 48-day period. As the tumors appeared to be shrinking, the right lower quadrant was then treated to a total dose of 5030 rads over a 66-day period.

The patient then did well for 11 months, at which time she noted rectal bleeding both around the stool and mixed with it. She was assured that this was not unusual, and no diagnostic or therapeutic steps were undertaken. Three months later, she con-

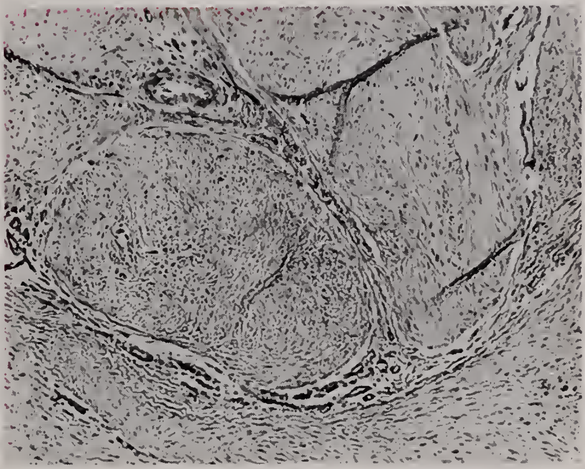

Fig. 1 — Desmoid tumor removed from abdominal wall. (x100)

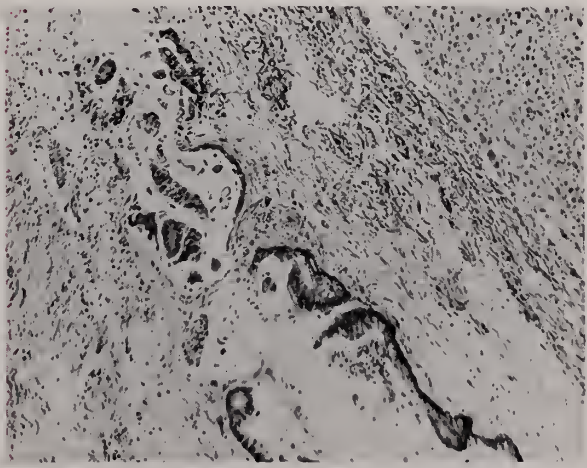

Fig. 2 — Liver biopsy demonstrating extensive fibrosis and replacement of hepatic tissue with adenocarcinoma. (x100)

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**See Test Your Word Score Page 1491.

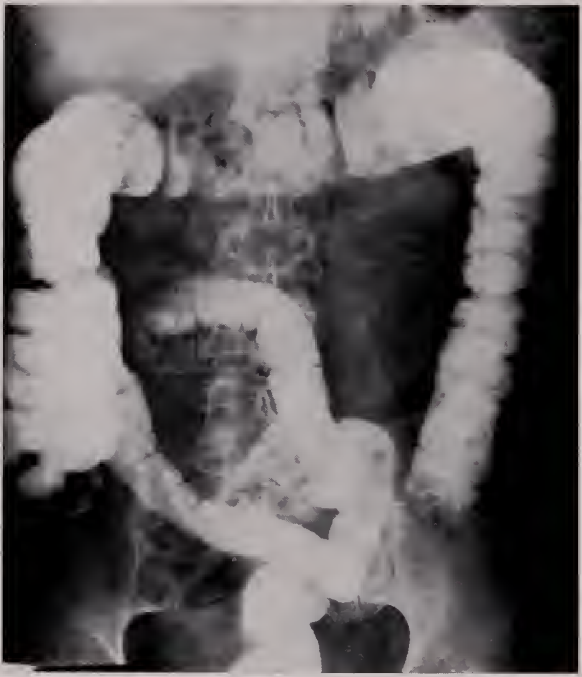

Fig. 3 — Barium enema demonstrating the multiple filling defects of polyposis.

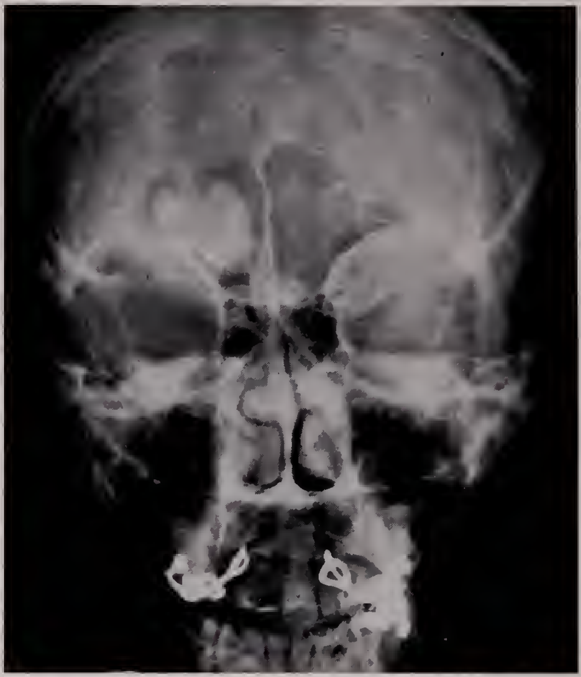

Fig. 4 — Radiograph of skull demonstrating large osteoma in frontal sinus. Also note extensive dental prosthetic devices.

sulted a proctologist who felt and visualized a large mass in her rectum. An exploratory laporatomy was done immediately, at which time carcinoma was found in multiple lymph nodes, the omentum, and both lobes of the liver (Figure 2). A transverse colostomy was performed to avoid obstruction of the colon. Multiple polyposis was observed in the colon.

She was informed of the metastatic nature of her disease and of the prognosis. Because of severe and almost constant pain, she elected to try a course of chemotherapy.

Physical examination at the time of admission revealed a frightened and cachectic young woman. Positive findings included exostoses over the skull, a hard nodular liver, and a rigid, indurated abdominal wall. There was a hard mass in the rectum, easily palpated, which was felt to be about 10 cm. in diameter. Vaginal examination demonstrated a "frozen pelvis" with this large mass almost obstructing the introitus.

Laboratory data included a normal urinalysis. Hematocrit was 30%. White blood count was 6,200 per cu. mm. with a normal differential. Blood urea nitrogen was 10 mgm%. Serum glutamic oxalacetic transaminase was 27 units. Alkaline phosphatase was 10.8 units. A barium enema demonstrated several polyps (Figure 3) in the distal colon. Radiographs of the chest were normal. Radiographic examination of the skull demonstrated a large osteoma in the frontal sinus (Figure 4).

Chemotherapy

The patient was started on intravenous 5-Fluorouracil, using the regimen of Ansfield,[3] with immediate reduction of pain and increase in well-being. The mass in her rectum has now shrunk approximately 60%. At the present time she has gained 12 pounds and requires almost no medication for pain. She has tolerated the medication well.

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We have forty million reasons for failure, but not a single excuse. — Kipling

A Safe Gastrostomy Tube for Infants

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THE EMPLOYMENT of gastrostomy tubes in infants is often necessary in a variety of conditions such as congenital esophageal atresia, esophageal perforation, corrosive stricture or neurogenic dysphagia. Although used as a temporary measure the type of tube chosen for the gastrostomy is critical. Whereas a Foley or Malecott catheter #18 or #20 French may be satisfactory and relatively safe in the normal adult stomach, the newborn infant presents a different problem, especially a premature infant with esophageal atresia, into whose stomach no fluid or food has ever entered. In this latter group the wall of the microstomach is very friable and soft and cannot long withstand continued pressure by any device without resultant full thickness necrosis and perforation. Any tube with a tip which could impinge on the gastric wall is thus potentially lethal. A #10 F or #12 F mushroom tip catheter, although safer to use than a Foley or Malecott catheter, has the disadvantage of a narrow lumen in proportion to outside diameter, predisposing to plugging by food. Thus it may be necessary to use a larger tube to gain lumen size; but a large gastrostomy in these infants carries the high risk of a gastrocutaneous fistula. Moreover, granted success when the gastrostomy tube is placed, the rigid tips of the tubes tend to dilate the gastrostomy tract when changed, again fostering a gastric fistula.

Mindful of and sadly experienced in the above complications, we have utilized without ill effects and without complication in both infants and adults, a soft, rubber Davol T-tube, size #12 F to #16 F, such as is routinely used for common bile duct drainage. These tubes are relatively thin-walled and soft, yielding a maximum inside diameter for over-all size, yet rigid enough to withstand the negative pressure of gastric suction and tissue pressure of the abdominal wall.

These tubes are prepared with short (1.5

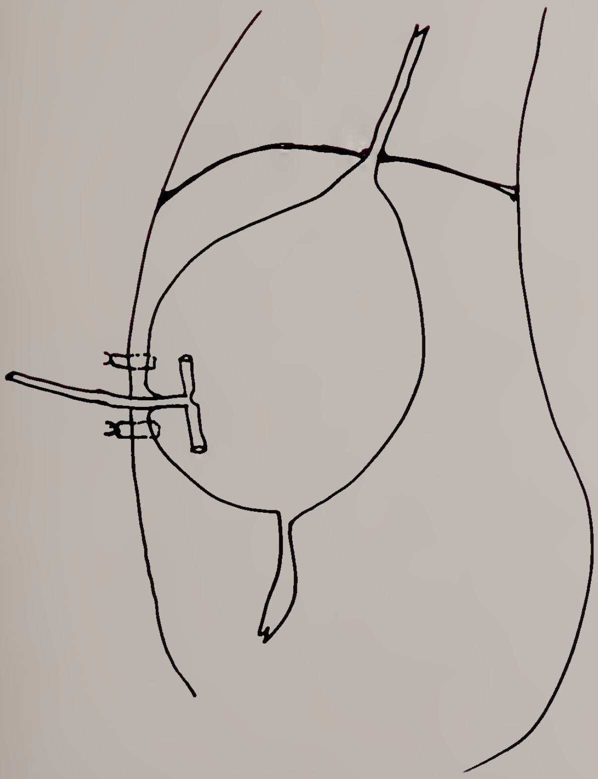

Fig. 1 — This is an outline drawing showing placement of the gastrostomy T-tube by the Stamm technique, emphasizing the subsequent suture fixation of the stomach to the anterior abdominal wall.

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cm.) transverse limbs, the tips of which are beveled away from the vertical limb, with a plug cut out of the transverse limb opposite the point of insertion of the vertical limb (Figure 1). The short limbs thus prepared are advantageous in several respects: 1) they facilitate ease of infusion of gastrostomy feedings with little likelihood of obstruction by coagulated feeding; 2) they are firm enough to resist moderate traction yet atraumatic when removed, thereby preventing dilation of the tract and predisposition to gastric juice leakage; and 3) there is no sharp rigid portion or tip of the tube to press on the gastric wall at any point, thus preventing gastric necrosis and perforation.

The T-tube is inserted into the stomach either with a Stamm technique, i.e., multiple concentric serosal purse-string sutures forming a serosa-lined tract perpendicular to the surface of the stomach, or with the Witzel technique, whichever is preferred. We have found however, that a Stamm gastrostomy utilizing the above described T-tube can be easily performed in the newborn through a small upper abdominal incision under local anesthesia. Upon insertion the limbs of the tube are pulled gently against the anterior gastric wall without fear of pressure necrosis of either the anterior or the posterior gastric wall. The vertical limb of the tube is finally secured by a catgut suture in the gastric wall and is passed through a stab wound in the abdominal wall lateral to the incision; then the stomach is sutured to the abdominal wall at the point of exit.

In addition, we are careful to utilize monofilament stainless steel wire to fix the T-tube to its point of exit from the skin. Moreover, we instill in the tube twice daily 5 cc. of a solution of 100,000 units of varidase at the completion of a feeding, thereby preventing coagulation of the formula upon the inner lining of the tube.

IT'S THE LAW

Surgeon's Fee Reduced by Court

In a suit by an orthopedic surgeon against an insurance company to recover a fee of $4,325 for services rendered in treating a patient's arm, a trial court did not err in awarding only $1,275. There was sufficient evidence to support a finding that that amount was a reasonable fee in the case, a Louisiana intermediate appellate court ruled. The patient's arm was severely injured when it was struck by the propeller of a motorboat.

The orthopedic surgeon testified that he considered that his charge was entirely reasonable and he was corroborated in this by another orthopedic surgeon. Two other experienced orthopedic surgeons from the same area testified for the insurer. They stated, respectively, that $600 and $1,000 would have been reasonable charges for the services rendered in this case. The law is well settled that whenever a doctor's charge is contested as being unreasonable and excessive, it is within the province of a court to adjust it to conform to the charges prevalent in the area where the services were rendered. On the basis of the evidence presented, there was no palpable error in the trial court's finding that the orthopedic surgeon's charge was excessive, and its finding will, therefore, not be disturbed, the court said.

Loomis v. Travelers Insurance Company, 169 So.2d — Citation April 30, 1965. 544 (La., Dec. 7, 1964)

Conscience: an inner voice that warns us somebody is looking. — Mencken

Water Absorption

by Dog Intestinal Mucosa

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Much of the advance in our understanding of intestinal absorption has been gained in the past 15 years from the study of *in vitro* preparations. Nearly all such preparations, including that of Fisher and Parsons[1] (generally considered the first of the satisfactory ones), have employed as a membrane the entire intestinal wall of rodents (rat, hamster, guinea pig). In the present investigation, membranes consisting of only the mucosa (epithelium plus lamina propria) of the small or large intestine of the dog were used successfully for the first time in the study of absorption. This paper will describe some aspects of the findings of these *in vitro* investigations, particularly as they relate to current theories of the mechanism of water absorption by the intestines.

Views of the Mechanisms of Intestinal Absorption of Water

Isotonic Water Absorption

Two observations challenging explanation are (1) absorption of water from isotonic NaCl or Ringer solutions or even from the animals own serum placed in the lumen (isotonic water absorption), and (2) absorption of water from hypertonic NaCl solutions. These processes can occur in the absence of a luminal hydrostatic pressure. In the first of the above observations, water is transported without an osmotic pressure difference, whereas in the latter, water is moved against the direction of the osmotic force. There is general agreement that active transport (transport driven by metabolic energy) by the epithelial cells is operating here in some way; this conclusion is supported by the dependence of the above kinds of water movement on the availability of oxygen and glucose (at least *in vitro*) and its inhibition by metabolic poisons. The main point of controversy is whether (a) Na^+ or Cl^- or both are absorbed actively with water following passively, or (b) water is absorbed actively.

Absorption of Water from Hypertonic Sodium Chloride

The second of the above observations, the absorption of water from hypertonic solutions, would superficially appear to be sufficient evidence for the occurrence of active water absorption, since water is being moved from low to high activity; moreover, the rates of absorption of sodium and chloride ions from hypo-, iso-, and hypertonic sodium chloride solutions placed in the dog intestines have been found to be consistent with a model providing for simple bulk flow and diffusion[2] without invoking active transport of sodium chloride.

Nevertheless, the most widely held view is that isotonic water absorption is a result of active sodium chloride absorption. The transported sodium chloride is thought to produce local relative hypertonicity on the blood side of the absorbing membrane, thus creating an osmotic driving force for passive water movement. The same process is presumed to operate for water absorption elsewhere in the body, as from the proximal tubule or the gallbladder. The essential bases for this view, so far as the intestine is concerned, appear to be first, evidence for the ability of the intestine to carry out active Na^+ transport,[3] second, the dependence of *in vitro* isotonic water absorption on the presence of Na^+ in the lumen,[3,4] and third, the nature of the calculated composition of the absorbed fluid (absorbate) during isotonic absorption. The most frequently cited relevant papers concerning the latter point are those of Curran and Solomon.[5,6]

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The question still remains as to how the theory of active sodium chloride absorption would account for water absorption from solutions as much as 100 mOsm/L hypertonic.[2] With an intact circulation, it is extremely unlikely that the required osmotic pressures could be maintained in the interstitial fluid of the villi. The answer given is exemplified by the two-membrane-in-series model proposed by Curran.[6] Space does not permit a detailed description of this idea. Suffice it to say that there is no theoretical difficulty, given the proper physical arrangements, in accounting for the observed water movement by active solute movement.

Water and Sodium Chloride Absorption by Dog Mucosal Membrane in Vitro

Results obtained on the isolated dog mucosal preparation will now be presented as they relate to the above discussion.

Method of Study

The surgical removal of the mucosal membrane, the apparatus employed for studying absorption, and conduct of the experiment have been previously described.[7] Figure 1 shows the membrane in the process of being stripped; Figure 2 shows a histological section of stripped mucosa. In brief, for the study of absorption, the membrane was tied

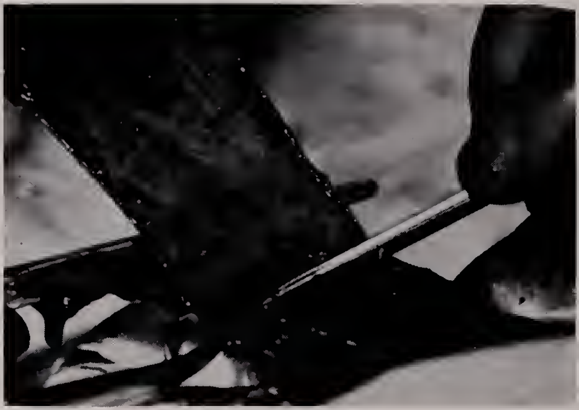
Fig. 1 — Dog mucosal membrane in process of being stripped.

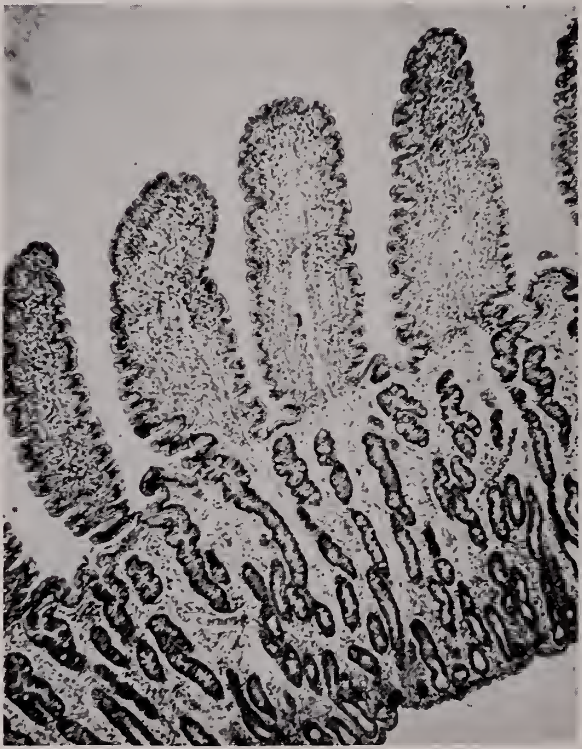
Fig. 2 — Histological section of stripped mucosa of small intestine.

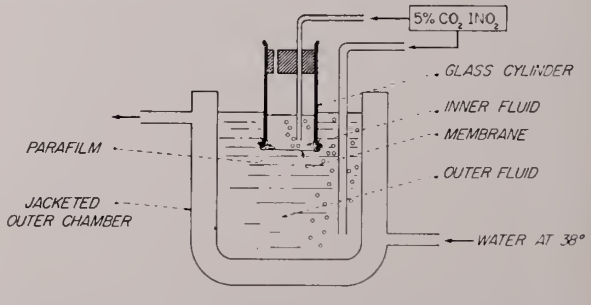

Fig. 3 — Arrangement for study of intestinal absorption.

on one end of a glass cylinder 6.4 cm^2 in cross sectional area, after which the membrane-covered end of the tube was immersed in a bathing fluid of large volume (about 200 ml.), as seen in Figure 3. Depending on the purpose of the experiment, the mucosal surface of the membrane faced either the large or small volume bathing fluid. The serosal bathing fluid was Krebs Bicarbonate Ringer, and all bathing fluids contained glucose. The Na^+ concentration in Krebs Bicarbonate Ringer was 146 mEq/L and the Cl^- concentration 127 mEq/L.

Water Absorption from Isotonic and Hypertonic Solutions

It was found that water was absorbed from isotonic Ringer fluid. The occurrence of this water absorption was largely dependent on the presence of glucose and oxygen in the medium, and it was prevented by suitable metabolic poisons. Furthermore, water was absorbed from Ringer fluids which were up to about twice isotonic. Transmucosal potential differences amounted to 5-13 mV, which is typical of other intestinal preparations *in vivo* and *in vitro*. It has been suggested that the electrical potential difference across the intestinal wall could provide the driving force for water transport by electro-osmosis.[4] However, the question would then arise as to the origin of the potential. It is usually attributed to active sodium transport.[3,8]

The above findings on this new *in vitro* intestinal preparation, supplemented by a number of others, such as active glucose transport and inhibition of water absorption by removal of Na^+ from the mucosal bathing fluid, provided evidence that it exhibited transport behavior expected of normal intestine.

Composition of the Absorbate

Representative data on the composition of the absorbate (Figure 4) show the relationship between sodium absorbed (J_{Na}) and water absorbed (J_w) from Ringer fluids, the osmotic activity of which was altered by changing their sodium chloride concentrations. The slopes represent the concentration of Na^+ in the water moved, corrected for solute movement which would occur with zero water movement. In each case, these slopes correspond to concentrations which were isosmotic with the luminal test solution (see legend of Figure 4). Similar results were obtained for Cl^-. The type of "coupling" between water and salt absorption is thus seen to be the same as has been reported *in vivo* for the intestine[2] and *in vivo* and *in vitro* for other absorbing organs, including the gallbladder.[9-11] The observations frequently considered more pertinent to the fundamental question of primary water versus primary sodium chloride absorption are those for the composition of the absorbate when a poorly absorbable solute osmotically replaces an appreciable portion of the Na^+, Cl^-, or sodium chloride of the Ringer fluids. Under such conditions, one or both of the ions, if absorbed, would be moved uphill. This leads us to the consideration of the phenomena of Cl^- and Na^+ impoverishment.

Impoverishment Phenomena

Chloride impoverishment by the intestine

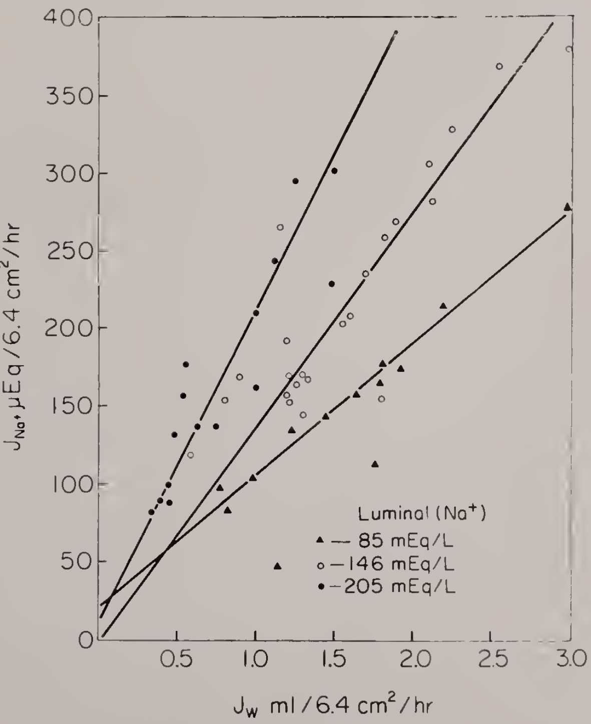

Fig. 4 — Relationship between absorption of sodium and water from Krebs Bicarbonate Ringer fluids, of varying sodium chloride concentrations. The lines have been visually fitted to the points. The slope of the lines are *83*, *130*, and *185* mEq/L respectively for the 85, 146, and 205 mEq/L luminal solutions.

refers to more rapid absorption of chloride relative to water from isotonic fluids with a chloride concentration less than that of the plasma. Typically, it has been studied in the dog from solutions ½ isotonic with respect to sodium chloride and Na_2SO_4 (the $SO_4^=$ being slowly absorbed relative to Cl^-). In the small intestine, it occurs most prominently in the ileum.[12] It has also been found *in vivo* in the rat and rabbit,[13] as well as in the dog.[12]

Sodium Impoverishment

Conversely, the analogous phenomenon, sodium impoverishment, occurs when $MgCl_2$ is used instead of the Na_2SO_4, and both Na and Cl impoverishment are found when a poorly absorbed nonelectrolyte replaces sodium chloride.[5,6] All the above *in vivo* impoverishment behavior was found to be exhibited in our *in vitro* preparation.

With respect to the composition of the absorbate during these various types of impoverishment experiments, the following observations were made. From solutions ½ isosmotic with respect to both sodium chloride and Na_2SO_4, the chloride absorbed was closely correlated with the water absorbed. For membranes taken from the lower 20% of the jejunum-ileum, as shown in Figure 5, the relationship appears to be reasonably linear, and the line fitted to these points has a nearly zero intercept. The slope of the line (the apparent Cl^- concentration in the fluid absorbed) is about 120 mEq/L and close to the Cl^- concentration in Krebs Bicarbonate Ringer. Thus, the 120 mEq/L in the solution moved originated from a luminal Cl^- concentration much lower in Cl^- (68 mEq/L). The Na^+ concentration in the absorbate was 160 mEq/L as compared with a luminal concentration of 190 mEq/L. The absorbate thus approximated an isotonic Krebs Bicarbonate Ringer fluid.

From ½ isotonic sodium chloride + ½ isotonic $MgCl_2$, despite the reverse situation with regard to luminal concentrations of Na^+ and Cl^-, the absorbate nevertheless again contained 160 mEq/L Na^+. The Cl^- concentration was somewhat higher, 148 mEq/L, than in the previous case. From ½ isotonic sodium chloride + ½ isotonic mannitol (Na^+ about 90 mEq/L and Cl^- about 68 mEq/L), with both ions moving against their concentration differences, the absorbate contained Na^+ = 142 mEq/L and Cl^- = 110 mE/L. Thus, in all these instances in which the luminal solutions were isotonic, the absorbate resembled isotonic Ringer fluid. These results are essentially the same as those on which Curran based his inference of primary active salt transport and secondary passive water transport.

Although the theories which postulate primary active water transport are not excluded by these findings, it is difficult to see how they can account for these phenomena in a simple way. In their conventional forms, these theories postulate either vesicular transport or some kind of fluid circuit, and both of these mechanisms would require rather demanding selective permeability properties for sodium chloride and other solutes. Therefore, if primary active sodium chloride and water transport are considered as mutually exclusive explanations of intestinal water absorption, active sodium chloride transport appears, in my opinion, to be the more likely one. It may of course turn out that contributions by active transport of both

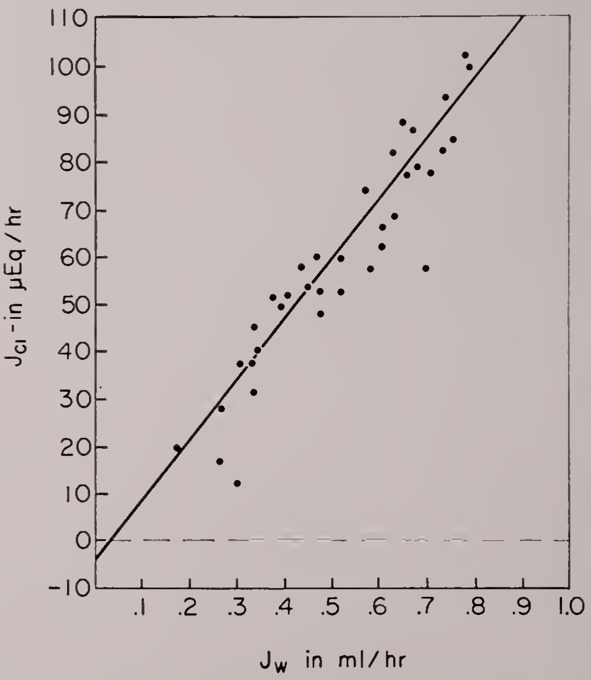

Fig. 5 — Relationship between absorption of chloride and water during the process of chloride impoverishment. The mucosal fluid was ½ isotonic sodium chloride + ½ isotonic Na_2SO_4.

are involved. In any event, the problem remains a fundamental one in the physiology of the intestine.

Importance of Convection in Intestinal Absorption

It is noteworthy that both of the contrasted theories imply a potential convective component in the absorption of any molecule. This component should appear most clearly in the case of small nonelectrolytes of low lipoid solubility for which the intestine has no special or active transport mechanisms.

The acceptance of the existence and importance of convective transport across cell and cellular sheet membranes has been largely due to Ussing; however, the evidence for its importance in intestinal absorption is relatively meagre. Among the most relevant investigations is that of Fisher,[14] who found that water movement and that of certain passively handled solutes were positively correlated. He concluded that such a process "as this coupled absorption must be the basis for absorption of the majority of drugs and foodstuffs, and (that) it may be supposed that physiological and pathological factors which affect water absorption will equally affect the absorption of this large class of solutes." In the literature, it is frequently assumed that the absorption of these substances is only by diffusion.

We studied this problem in great detail using urea,[15] D_2O,[15] thiourea, xylose, and antipyrine either *in vivo* or *in vitro* or both. We found that the convective component in the transport of these passively absorbed substances indeed had a dominating influence on the kinetics of solute movement during high rates of water absorption. This component manifested itself in an obvious way by causing absorption of these solutes against their concentration gradient, that is, in the direction opposite from that expected by diffusion.

Summary

The findings with this new preparation supplement those obtained on other preparations, which are viewed as favoring the theory that water absorption from isotonic or hypertonic solutions is passive and secondary to active sodium chloride absorption.

Findings are briefly described confirming the implication of the theories of water absorption that passive absorption of solutes should be in part convective.

The above work was performed in the Department of Physiology of the University of Minnesota Medical School in collaboration with Professor N. Lifson.

This work was supported in part by Public Health Service grants C-5538 (C-3) and AM-06700.

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Diplomacy is to do and say
The nastiest thing in the nicest way. — Isaac Goldberg

Who can remember when you bought $5 worth of groceries and had to hold the bag from the bottom? — Changing Times

Pseudocysts

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ALTHOUGH PSEUDOCYSTS of the pancreas are not common lesions, they are the source of prolonged morbidity and possibly even death if not properly treated. For this reason the nature of these lesions and the techniques available for their treatment are worthy of review. In the discussion to follow pseudocysts are considered collections of necrotic tissue, blood and pancreatic juice in the lesser sac of the peritoneal cavity occurring as sequelae of pancreatitis or pancreatic trauma. False cysts due to other causes and true cysts or cystic tumors of pancreas will not be considered.

There may be a history of pancreatitis or blunt abdominal trauma followed within a period of weeks to months by the appearance of a slowly enlarging mass in the left upper part of the abdomen. In some patients no antecedent history of pancreatic inflammation or trauma can be elicited. Symptoms related to pressure on the stomach or gastric outlet obstruction may be present or the mass may be symptomless. Laboratory studies are usually not helpful. Radiographic examinations with and without contrast media demonstrate a mass displacing the stomach anteriorly; often the colon is displaced downward (Figures 1 & 2). With a clear-cut history of antecedent blunt trauma or pancreatitis the diagnosis is fairly obvious. In the absence of such a history it is possible only

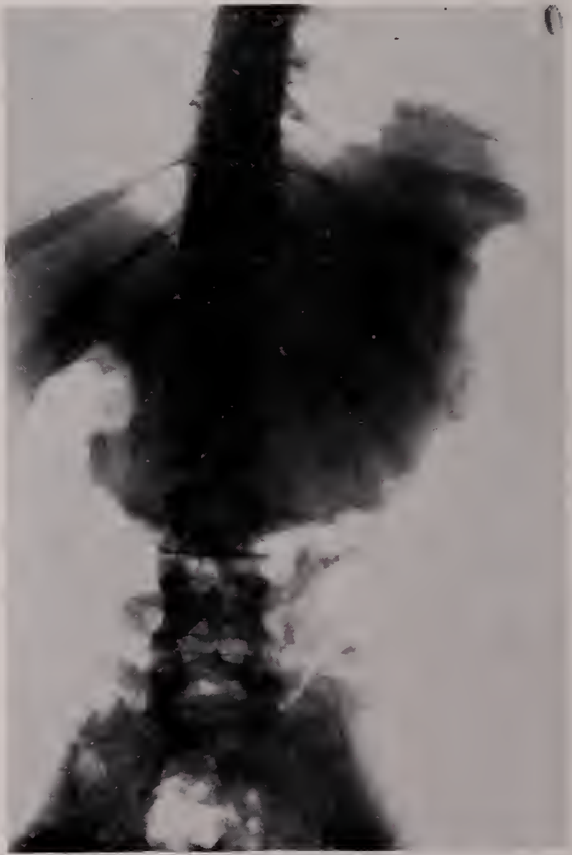

Fig. 1 — Supine radiograph showing mass in left upper quadrant.

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of the Pancreas

to suspect such a lesion.

Surgical exploration is indicated. Gross appearance of a pseudocyst at operation is characteristic. There is a fluid-filled mass palpable behind the stomach, but attempts to approach the mass are met by dense adherence of visceral structures on all sides. The mass may lie predominantly in the upper or lower part of the lesser bursa, and part of the lesser sac may be obliterated. Location of the mass in part determines its proper treatment. Wall of the cystic structure consists of the surrounding stomach, pancreas, transverse colon and omentum, and it is obvious that such a structure cannot be excised. It is important that the true character of the lesion be recognized and its benign character established by (1) its characteristic location, (2) aspiration which demonstrates a brown muddy fluid consisting of necrotic tissue, blood and pancreatic juice, and (3) biopsy of the wall at the site decided upon for drainage. Once it has been entered, the wall of the false cyst will be found to consist of fibrous tissue, fibrin and a coagulum of digested blood applied to visceral strictures. On entering the cyst with other than an aspirating needle care must be taken to avoid opening the stomach, colon or small bowel which are adherent to it. It is usually possible to reflect the omentum from the transverse colon sufficiently for aspiration and determination of the proper site for draining the pseudocyst.

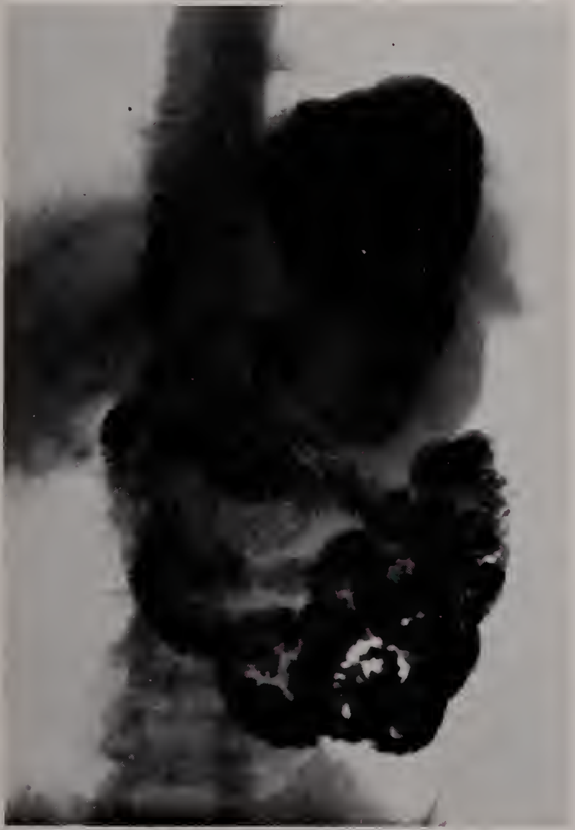

Fig. 2 — Upper gastrointestinal study with barium showing stomach displaced anteriorly by a mass.

Surgical Procedures for Treatment of Pseudocysts

Techniques employed for management of pseudocysts are given in Tables 1 and 2, and the advantages and disadvantages of each will be briefly discussed.

Marsupialization and External Drainage*

First described in 1883 by Gussenbauer,[1] variations of this technique remained the standard method of treatment for many years. Some pseudocysts communicate with the pancreatic duct system by large openings; in others the accumulation in the lesser sac has come from much smaller communications. If pseudocysts have the former type of communication or if there is obstruction in the pancreatic ducts, prolonged drainage, cyst recurrence, excoriation of skin and electrolyte imbalance have occurred. Reoperation has been necessary in one fourth of the cases.[2] For cysts with small communications and no duct obstruction, closure can be expected with external drainage, since pancreatic secretions do not continue to be poured into the cyst. Unfortunately, without pancreatography it is not possible to demonstrate which cysts have functional communications and which do not. Since there are more satisfactory techniques for dealing with pseudocysts, external drainage alone is no longer an acceptable operation.

Cystgastrostomy

Cystgastrostomy with resection of part of the cyst represented the earliest effort at internal drainage.[3] An improvement was cystgastrostomy by a transgastric approach.[4] In this latter operation an incision is made in the anterior wall of the stomach, and that portion of the posterior gastric wall which overlies the pseudocyst is incised and the cyst opened. A running suture for hemostasis is placed around the opening in the posterior gastric wall, and the anterior wall of the stomach is closed in layers. This operation has many advocates, but a few authors have condemned it because of passage of gastric contents into the cyst,[5,6] with resulting pancreatitis[6] and hemorrhage.[7,8] Cystgastrostomy may be useful for those cysts lying high in the lesser bursa which are not easily accessible for drainage into the small bowel.

Cystduodenostomy[9]

For pseudocysts which present anterior to the head of the pancreas, anastomosis has been constructed between the cyst wall and duodenum. Such a procedure is advantageous if a fistula from the pancreatic duct persists so that pancreatic juice drains into the duodenum. A theoretical disadvantage of the operation is regurgitation of gastric juice, food and bile into the cyst. The operation would appear to have a very limited role in the treatment of pseudocyst.

Cystjejunostomy

Anastomosis of the cyst to the jejunum has been accomplished by several methods: simple cystjejunostomy,[10] cystjejunostomy with jejunojejunostomy,[11] transvisceral cystenterostomy,[12] cystjejunostomy Roux-en-Y,[13]

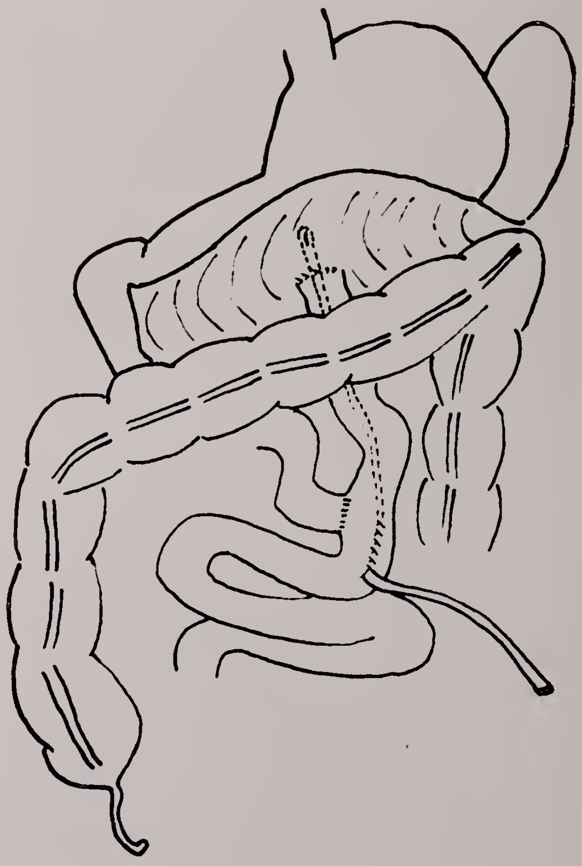

Fig. 3 — Modification of Roux-en-Y cystenterostomy by addition of catheter enterostomy.

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[*] See Test Your Word Score Page 1491.

and cystjejunostomy Roux-en-Y with catheter enterostomy.[14]

Simple cyst jejunostomy would seem to have the same disadvantages as cystgastrostomy, namely, that intestinal contents would enter the cyst cavity. In a collected series of 32 patients in whom simple cystjejunostomy had been used, Warren and associates[2] found that five deaths (15.6%) occurred and two reoperations were required.

Transvisceral cystenterostomy has been utilized when the small bowel forms part of the cyst wall at some point. Drainage is accomplished by opening the intestine, then creating a stoma between cyst and bowel at the point of adherence, followed by closure of the bowel. Regurgitation will occur after this operation, and it appears there will be few circumstances when adherent intestine can be utilized in this manner to drain a pseudocyst.

Cystjejunostomy Roux-en-Y has been extensively employed.[2] The advantage of this operation or of cystjejunostomy with jejunojejunostomy lies in a provision for keeping intestinal content away from the cyst cavity. In a series of 46 cases there was an over-all 2.2% mortality rate, and two reoperations were necessary.[2] Breakdown of anastomosis,[2] intestinal hemorrhage[15] and recurrent cyst[15] are complications which have been attributed to this procedure. Shumacker[16] in 1954 reported five patients treated by this procedure and found a total of 17 cases in which the operation had been performed successfully.

We have modified this procedure by addition of catheter enterostomy. By external drainage through the catheter it is possible to keep the cyst decompressed until firm union has occurred between cyst wall and jejunum. The catheter enterostomy poses no problem and in addition allows assessment of cyst size by instillation of radio-opaque media at intervals until the cavity is obliterated when the enterostomy tube is removed. In those cysts which close without a permanent fistula it will be necessary to determine whether the blind loop created by Roux-en-Y drainage procedure is associated with any of the complications which have been attributed to blind intestinal loops under other circumstances.

Implantation of Fistula into Jejunum after External Drainage[17]

Application of this operation is limited to patients previously treated by external drainage with a persistent external pancreatic fistula. Under these circumstances it may be possible to amputate the fistulous tract as close to the body of the pancreas as possible and anastomose it to the jejunum. For external fistulas, some direct attack on the pancreatic duct system as described below is probably better.

Sphincterotomy with Concomitant External Drainage[17]

Advocates of this procedure have concluded that patients with pseudocysts of inflammatory origin have spasm of the sphincter of Oddi which tends to perpetuate or increase the size of the cyst. Drainage would be expected to persist because spasm causes pancreatic intraductal pressure to be higher than normal. Sphincterotomy was proposed not only in treatment of the inflammatory cyst but to prevent recurrent pancreatitis. The demonstration that obstructions in the pancreatic duct in pancreatitis are often multiple and not limited to the sphincter of Oddi indicates such an approach is not applicable in all patients with pseudocyst. Before treatment of pseudocyst by sphincterotomy and external drainage it would be necessary to demon-

TABLE 1

Surgical Procedures for Treatment of Pseudocyst of the Pancreas

1. Marsupialization and External Drainage.
2. Cystgastrostomy.
3. Cystduodenostomy.
4. Cystjejunostomy.
5. Implantation of Fistula into Jejunum.
6. Sphincterotomy with Concomitant External Drainage.
7. Retrograde Transductal Internal Drainage.

TABLE 2

Cystjejunostomy in Treatment of Pseudocyst of the Pancreas

a) Simple Cystjejunostomy.
b) Cystjejunostomy with Jejunojejunostomy.
c) Cystjejunostomy Roux-en-Y.
d) Cystjejunostomy Roux-en-Y with Catheter Enterostomy.

strate by radiographic visualization of the pancreatic duct a definite communication between cyst and duct and no obstructions of the duct. If these criteria are met the concept appears sound in principle.

Retrograde Transductal Internal Drainage

Menguay and Blalock[18] have reported a patient with a pseudocyst lying over the head of the pancreas and behind the antrum and the first portion of duodenum who was treated by amputation of the tip of the tail of the pancreas, by opening of the pancreatic duct, and by creation of a large stoma between cyst and duct by an instrument introduced into the cyst through the duct. The tail of the pancreas was then anastomosed to a Roux-en-Y loop of jejunum. Such an operation for draining the cyst into the pancreatic duct would be applicable only to those pseudocysts overlying the pancreatic head. It would appear to be a more difficult operation than others.

Discussion

In patients with pseudocyst of inflammatory or traumatic origin internal drainage is preferable to external. A number of operations have been proposed to accomplish internal drainage. Basically they fall into two general categories: (1) Those procedures wherein the cyst is anastomosed to the gastrointestinal tract. No direct attack is made upon the pancreas itself, and if a fistula from the pancreatic ductal system persists, secretions will enter the alimentary canal. Such an approach does nothing for the underlying pancreatic disease in the case of post-inflammatory pseudocyst and recurrent cyst formation and pancreatitis after cyst enteric anastomoses have been described.[17] (2) Procedures designed to drain the pseudocyst into the pancreatic duct. Operations such as those described by Doubilet and Mulholland[17] and Menguay and Blalock[18] fall into this category. Provided the possibility of multiple sites of occlusion in the duct system is considered, the basic principle of such procedures is sound. Unless at least a part of the pancreas and its ductal system is accessible and unless the surgeon is skilled in such operations, cyst enteric drainage is probably the preferred approach. Except under a few circumstances mentioned before, cystjejunostomy Roux-en-Y is probably the operation most likely to give a satisfactory result.

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Daylight saving is founded on the old Indian idea of cutting off one end of the blanket and sewing it on the other end to make the blanket longer. — Gas Flame

Never give a child a choice. Don't give him a choice of believing in God or not. He can start having choices when he goes to college. — Robert Frost

Hematuria
in
Sickle
Cell
Disease

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HEMATURIA OCCURRING in patients with sickle cell disease was first reported in 1948. Although many cases have now been reported, general awareness of this phenomenon has been poor. At Ancker Hospital we recently encountered a patient who pointed up this problem; and although the negro population of St. Paul and Ramsey County is small, the diagnosis of sickle cell hemoglobinopathy has been made in 62 patients during the last five years. In all instances the diagnosis was based on either positive sickling preparations or hemoglobin electrophoresis. A review of these 62 patients has revealed eight with gross hematuria for which there was no other explanation. Four of these patients will be presented in some detail.

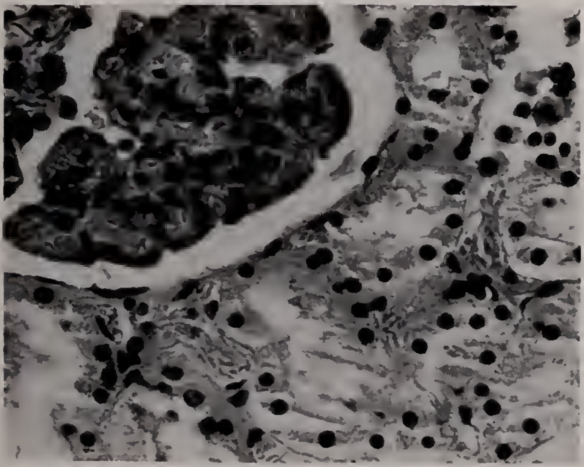

Fig. 1 — Post-mortem histology of kidney showing intense congestion and sickling of erythrocytes. (x600)

Case Reports

Case 1.

An 18-year-old negro male entered Ancker Hospital because of painless gross hematuria which began following a wrestling match. He denied severe bruises but did relate minor flank trauma during the bout. He was not anemic. Urinalysis was normal except for gross blood. Multiple studies for renal disease were negative. Cystoscopy demonstrated bloody efflux from the left ureter. An intravenous pyelogram was normal except for clots in the renal pelvis. Cultures of the urine for routine pathogens, Mycobacteria, and fungi were negative. Bleeding and clotting studies, vascular fragility, and platelet counts were normal. A sickle cell preparation was positive, and electrophoresis of his hemoglobin solution demonstrated S and A hemoglobins. Treatment was conservative and bleeding ceased after 36 days.

Case 2.

A 49-year-old negro female began to pass bright red blood per urethra during an episode of bronchitis. She stated that a previous similar episode had occurred in 1940. She was told then that she had a tumor in her left kidney, but no surgery was done. Cystoscopy demonstrated brisk bleeding from the left ureter. An intravenous pyelogram revealed a mass in the left renal pelvis which was felt to be either a tumor or blood clots. Cultures were negative. She was not anemic. A sickle cell preparation was positive, and electrophoresis of her hemoglobin demonstrated a mixture of S and A hemoglobins. Bleeding ceased after 10 days of bed rest. Subsequent pyelograms have been normal.

Case 3.

A 53-year-old negro male began passing gross blood per urethra one week after the onset of pneumonia. He was not anemic. Urinalysis was normal except for blood. A sickle cell preparation was positive, and electrophoresis demonstrated S and A hemoglobins. As he ceased bleeding after three days, no further studies were undertaken. A subsequent intravenous pyelogram was normal. He died one month later of a myocardial infarction. Post-mortem examination revealed only congestion of his kidneys with sickled erythrocytes in the renal vessels (Figure 1).

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Case 4.

A 37-year-old negro female is the mother of nine children, including seven children with sickle cell hemoglobinopathy. She is not anemic but has been seen in the Ancker Receiving Room on multiple occasions complaining of arthralgia and abdominal pain. She is alleged to imbibe to considerable excess and for prolonged periods of time. During one such episode of ethanolic* debauchery she began to pass red blood in her urine. This continued for three weeks, at which time she was admitted to Ancker Hospital. Bleeding ceased shortly after admission. Cystoscopy was performed but no bleeding site could be localized. Studies for infection were negative. An intravenous pyelogram was normal. A sickle cell preparation was positive and electrophoresis demonstrated a mixture of S and A hemoglobins.

A summary of our eight patients is presented in Table 1. The ages range from 18 to 54 years. There are four females and four males. Hemoglobin electrophoresis has been performed in five, all of whom have SA hemoglobin. Bleeding was localized in two instances, both from the left ureter. Duration of bleeding was variable but stopped in each instance without surgical intervention. Of particular interest is the fact that many of these patients had some event that could conceivably have precipitated a crisis of in vivo sickling. It is well known that patients with SA hemoglobin may have considerable difficulty if the oxygen tension of their blood is lowered or if stasis occurs in their venous system. Thus it may be significant that hematuria occurs following bronchitis, pneumonia, smoke inhalation, congestive heart failure, or even the sound slumber following the ingestion of large amounts of spiritus frumenti.*

TABLE I

Summary of Ancker Patients

Age	Sex	HGB	Sickling	Location	Duration
18	M	SA	+	Left	36 days
49	F	SA	+	Left	10 days
53	M	SA	+	?	Brief
37	F	SA	+	?	21 days
40	F	SA	+	?	Intermittent
26	F	?	+	?	Brief
46	M	?	+	?	10 days
43	M	?	+	?	Intermittent

Review of Literature

Shortly after Abel and Brown[1] reported hematuria in a young negro soldier with sickle cell disease, other cases began to be recognized and reported. It became apparent that this was not an uncommon manifestation of sickle cell disease. There have been 152 cases reported in varying detail.[1-16] Table 2 is a summary of these patients who were reported in sufficient detail for tabulation.

Electrophoretic analysis of hemoglobin solution was performed in 76 patients. Of these, 54 had SA hemoglobin, 21 had SC hemoglobin, one patient had sickle cell thalassemia and one SS hemoglobin. When these figures are compared with the frequency of each hemoglobin type, there is a slight preponderance of SA and SC hemoglobin types. No reason is apparent for this preponderance.

Of particular interest is the site of bleeding in these patients. Bleeding was localized in 113 patients. Of these, 77 bled from the left kidney, 32 bled from the right, and four bled from both kidneys. This represents a significant difference for which there is no physiologic explanation. It is of interest that early reports were of bleeding from the left side, while later reports are of bleeding from the right side. Perhaps future reports will effect a balance between right and left.

Sex was identified in 136 patients. There were 86 males and 50 females. Recent reports show females in predominance, so that a balance may be achieved here as well as in location. A reasonable explanation for these variations may be that early reports were almost exclusively from the Armed Forces. In this situation the cases would be selected from young adult males who were healthy enough to be inducted.

Duration of bleeding is highly variable. Most patients bleed only a few days, but some are reported who have bled almost continuously for over 10 years. The average duration is two to three months. Intermittent bleeding is common, and recurrences are almost universal. One patient had severe bleeding, recovered, and then had a recurrence 30 years later.

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*See Test Your Word Score Page 1491.

The age at the time of bleeding ranges from five to 70 years, with a sharp peak between ages 25 and 35.

Pathogenesis

Sickle cell disease may be divided into several categories on the basis of electrophoresis and chromatography of hemoglobin solutions. The severity of anemia and frequency of crisis correlates roughly with the per cent of S hemoglobin present. Most patients with SA hemoglobin have less than 50% S hemoglobin and have very little, if any, trouble. However, under conditions of decreased oxygen tension they do have difficulty. They may, for example, have a typical crisis following high altitude flight.[17]

The phenomenon of hematuria does not follow the usual guidelines. In the earlier reports, a large majority of patients with hematuria began bleeding following a long march or minor flank trauma. Later reports have emphasized bronchitis, pneumonia and congestive heart failure as precipitating events. One of our patients, a fireman, began to bleed following smoke inhalation.

Anatomic study of the kidneys is not helpful in terms of etiology.[18,19] There is congestion of vessels with sickled erythrocytes and erosion of the pelvic mucosa. Rarely is papillary necrosis seen.

Renal physiologic studies in patients with sickle cell disease demonstrate increased glomerular filtration rate, effective renal blood flow, and tubular excretory capacity.[20] In addition, there is some impairment of concentrating ability, so that hyposthenuria* is common.[21] However, these aberrations do not explain why bleeding begins. The oxygen tension in renal capillaries is low enough to favor sickling. Presumably, every patient with sickle cell disease has sickled erythrocytes in renal capillaries. A reasonable hypothesis is that this physiologic state favoring sickling, when coupled with trauma or con-

TABLE 2
Review of Literature

Reference	Age	Sex	HGB Type	Location	Duration in Days	Recurrences
1	26	M	—	Left	10	—
2	43	M	—	Left	10	2
2	27	M	—	Left	2	—
2	54	M	—	Left	14	1
2	32	M	—	Left	5	—
2	35	M	—	Right	26	- -
2	35	M	—	Left	5+	Intermittent
2	31	M	—	Left	120+	Intermittent
3	30	M	SA	Left	21	—
4	28	M	—	—	3+	—
4	—	—	—	—	—	—
5	35	M	SC	Left	—	3
5	16	F	SC	Left	—	—
6	19	M	—	Left	120+	—
6	34	M	—	Right	—	Intermittent
6	11	M	—	Left	1000+	Intermittent
6	23	F	—	Right	—	6+
6	44	F	—	—	—	3+
6	34	M	—	Left	42+	—
6	41	F	—	—	—	—
7	12	M	SC	—	—	—
7	22	M	SC	—	—	—
8	42	M	—	Left	—	—
8	33	M	—	Left	—	—
8	28	F	—	Left	—	Intermittent
8	31	F	—	Right	—	—
8	26	F	—	Left	—	—
8	40	F	—	Left	—	—

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*See Test Your Word Score Page 1491.

TABLE 2 (Continued)

Reference	Age	Sex	HGB Type	Location	Duration in Days	Recurrences
8	27	M	—	Left	—	—
8	14	M	—	Left	—	—
8	10	M	—	Right	—	—
9	38	M	SA	—	1000+	2
9	30	M	SA	—	1800+	Intermittent
9	24	M	SA	Right	700+	Intermittent
9	17	M	SA	Left	300	—
9	27	M	SC	Right	—	—
9	41	M	SC	Left	700	—
9	25	M	SC	Left	—	2
9	29	M	SA	—	—	—
10	26	M	SC	Left	4	2
10	13	M	SC	Left	4	—
10	17	F	SC	Left	14	—
10	37	F	SA	Right	365	—
10	35	F	SA	Left	30	—
11	22	M	—	Left	42	Intermittent
11	54	M	—	—	—	—
12	26	M	SA	—	—	Intermittent
12	22	F	SA	Right	30+	Intermittent
12	19	M	SA	Right	30+	—
12	24	M	SA	—	—	—
12	19	M	SA	Both	30+	Intermittent
12	22	F	SA	—	2	Intermittent
12	39	M	SA	—	—	—
12	30	M	SA	Left	—	—
13	21	M	—	Right	60	Intermittent
13	24	F	—	—	—	—
14	26	M	—	Left	—	Intermittent
14	28	M	—	—	—	Intermittent
14	26	M	—	Left	—	—
14	27	M	—	Left	1200+	Intermittent
14	38	M	—	Left	7	—
14	31	M	—	—	—	Intermittent
14	30	M	—	Left	—	2+
15	21	M	SA	Right	700	—
15	24	F	SA	Right	350	—
15	18	F	SC	Left	1	—
15	29	F	—	Right	14	Intermittent
15	37	F	SA	Right	2	—
15	60	M	SA	—	21	—
15	46	F	SC	Right	4	3
15	47	F	—	—	—	—
15	53	M	—	Right	—	—
15	25	F	SA	—	—	—
15	35	F	SA	Right	—	—
15	34	M	SA	Left	10	2
15	34	F	SA	Left	3	Intermittent
15	28	F	SA	Right	150	—
15	29	F	SA	Both	5	2
15	27	F	SA	Both	—	Intermittent
15	15	M	—	Both	6	1
15	25	F	—	Left	5	Intermittent
15	31	F	SA	Left	6	—
15	18	M	SA	—	—	—
15	21	F	—	Right	4	—
15	40	F	SA	Right	—	—
15	18	F	—	Left	15	Intermittent
15	44	F	SA	Left	3000+	Intermittent
15	17	M	SS	Left	1	1
15	57	M	SC	Left	2	1
15	26	F	SA	Left	2	—
15	29	M	SA	—	1	—
15	29	F	SA	Right	1	—

gestion, initiates a vicious cycle of stasis and sickling resulting in hematuria.

Treatment

There is no specific treatment for sickle cell disease. Many therapeutic modalities have been employed with no success. Oxygen does not appear to be effective but is still used in an effort to reduce sickling. Hematuria associated with sickle cell disease almost always stops spontaneously. Nephrectomies were done a few years ago but were usually followed by bleeding from the other kidney. Bed rest and transfusions as necessary seem to offer the best approach to this problem. Since recurrences are common, nephrectomy should be avoided at all cost.

Summary

Hematuria, associated with sickle cell disease, is not uncommon. During the last five years, eight patients with this syndrome have been seen at Ancker Hospital.

There have been 152 cases reported in the literature. There is a preponderance of SA and SC hemoglobin in these patients. Bleeding may recur several times or may be persistent for years. Reports show a predominance of males with bleeding from the left side.

The etiology of hematuria in patients with sickle cell disease is unknown.

Treatment should be conservative since bleeding tends to stop spontaneously and may recur after nephrectomy.

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13-21 May be secured from the author or the reprints.

PANCREATIC MALIGNANCY SYNDROME

This syndrome presents a diagnostic triad of (1) progressive obstructive icterus; (2) large palpable gallbladder (Courvoisier's sign*), and (3) rapid, progressive cachexia.

Anorexia, rapid weight loss and night pain are the usual symptoms. A decrease in the enzyme concentration in the duodenum results in an impairment of glucose metabolism with hyperglycemia and a marked increase of neutral fat in the stool. Serum lipase is increased and the serum bilirubin becomes elevated. A barium X ray may show a widened duodenal loop, and multiple venous thrombophlebitis migrans is a common complaint. The course is rapid and the outcome fatal, with a poor prognosis from surgery.

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*See Minnesota Med 47:789, 1964.

Fiction is a beguiling wench for the bewildering roulette of life. — Lea Rosten

Trepopnea[*] a Possible Cause for Unilateral

WHILE THE radiographic picture of pulmonary edema is usually that of ill-defined confluent mottled shadows which fan symmetrically from both hila and spare the periphery of the lung,[1] pulmonary vascular congestion may appear as unilobar, multilobar, nodular or miliary infiltrations which simulate metastatic or primary malignancy, bronchiectasis, pneumonia, tuberculosis, uremic pneumonitis or pulmonary infarction.[2-8] The purpose of this report is to present a case of pulmonary edema which was radiographically confined to the right thorax and to comment on a possible cause.

Case Report

An 85-year-old white woman, was admitted to D. C. General Hospital on February 2, 1963, because of shortness of breath.

Past History

The patient had been without known heart disease until 17 years prior to admission when she was admitted to another hospital because of a "heart attack" and a "slight stroke," which were manifested by ill-defined chest pain and transient hemiparesis respectively. Since that hospital admission she had had orthopnea, slight dyspnea on exertion, and occasional substernal chest pain relieved by nitroglycerine. *For an unknown period of time she was unable to lie on her left side because of dyspnea incurred in that position.*

For the two years preceding admission, she had been confined to a nursing home because of blindness and inability to care for herself and, therefore, spent much of her time at bedrest and on her right side.

Present Illness

Two weeks prior to admission the patient developed an upper respiratory infection characterized by coryza and cough productive of whitish nonfoul-smelling, but occasionally blood-flecked sputum. Concomitantly she noticed progressive shortness of breath and frank episodes of paroxysmal nocturnal dyspnea. For the two nights prior to admission she had been unable to sleep at all because of dyspnea and wheezing. A roentgenogram taken on admission was read as compatible with right upper lobe pneumonia or tuberculosis. There was no history of chills, fever, hypertension, pleuritic chest pain, anorexia, nausea, or vomiting.

Physical Findings

Physical examination on admission revealed an elderly, alert white woman in moderate respiratory distress lying on her right side. Blood pressure was 130/90, pulse 90 and irregular, temperature 98.6 and respirations 28. Bilateral corneal opacities were present. The neck veins were distended at thirty degrees and filled from below. The right chest revealed inspiratory crackling rales to the level of the scapula and scattered expiratory rhonchi at the right base, while the left chest was relatively clear. On auscultation of the heart, an irregularly irregular rhythm and a ventricular diastolic gallop were heard, with the aortic component of the second sound louder than the pulmonic. A grade II systolic murmur was heard at the apex which radiated to the left sternal border. Examination of the abdomen revealed a positive hepatojugular reflux and a smooth, nontender liver palpable three fingers below the right

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[*] See Test Your Word Score Page 1491.

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Pulmonary Edema

costal margin in the midclavicular line. There was no peripheral edema, clubbing or cyanosis.

Laboratory Findings

The admission laboratory data revealed a hematocrit of 49, a white blood cell count of 7700 per cu. mm. with a normal differential count, and a urine with a specific gravity of 1.018 and two to three white cells per high power field. The fasting blood sugar was 85 mgm. %, and the blood urea nitrogen 40 mgm. %, the latter falling to 14 mgm. % at the time of discharge. The electrocardiogram showed atrial fibrillation. The admission chest roentgenogram showed cardiomegaly and a mottled shadow fanning out from the right hilum and involving most of the right hemithorax (Figure 1a). Tuberculin and histoplasmin skin tests were negative. Sputum smear was unremarkable, while sputum culture grew Neisseria catarrhalis and alpha hemolytic streptococci. Three twenty-four hour sputum specimens showed no tubercle bacilli.

Treatment

The patient was treated with digoxin and Mercurhydrin.[c] Twenty-four hours after admission she had lost three pounds and was no longer dyspneic. A chest roentgenogram on the third hospital day showed almost complete clearing of the right-side infiltration (Figure 1b). Her cough and coryza cleared, and she remained afebrile during her hospital stay. She lost a total of six pounds and was discharged without symptoms on the fourteenth hospital day.

Discussion

The clinical diagnosis of unilateral pul-

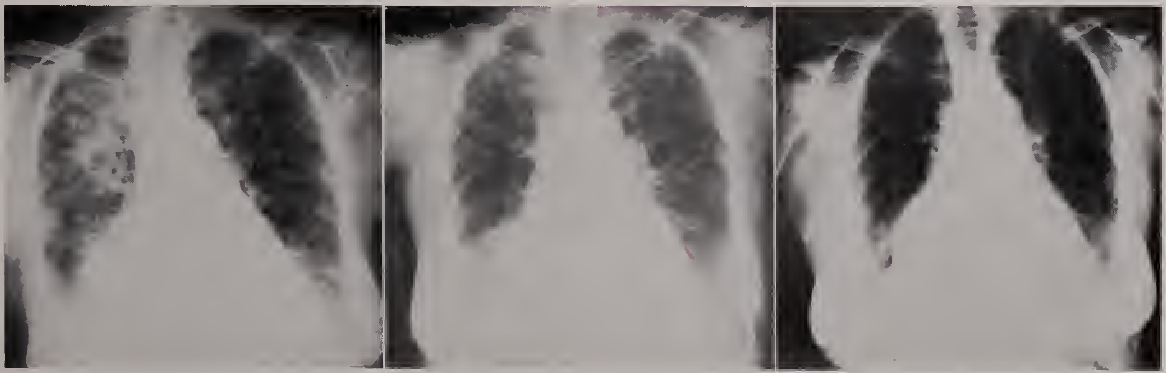

Fig. 1 — (left) Admission X-ray showing cardiomegaly and diffuse infiltration involving most of the right hemithorax. (middle) Follow-up film revealing almost complete clearing of the right-sided infiltration taken forty-eight hours after admission. (right) Film taken six days after admission showing complete clearing of right-sided shadow.

monary edema was substantiated in this patient by rapid roentgenographic clearing. Of the conditions which it may simulate, only pulmonary vascular congestion clears as rapidly. Moreover, the clearing was concomitant with the administration of a mercurial diuretic, and the patient had no findings (fever, positive sputum culture) suggestive of pneumonia. The degree of nitrogen retention was not at the level usually associated with uremic pneumonitis. Finally the majority of unilateral radiographic manifestations of pulmonary edema were confined to the right chest.[2-8]

It seems reasonable to assume that the patient's preference for the right lateral decubitus position played a major role in the radiographic localization of pulmonary edema in an individual confined to bed in a nursing home because of blindness. Increased hydrostatic pressure induced by gravity potentiates intra-alveolar extravasation of fluid in a manner analogous to the occurrence of pedal edema in dependent extremities.[9,10]

Right-sided preference, because of distressing symptoms incurred on the contralateral side, is not uncommon in individuals with congestive heart failure. In one study of 52 such patients, only two preferred sleeping on their left side.[11] This phenomenon is called trepopnea (literally, to turn to breathe). While the reason for it is unknown, right-sided preference appears to be correlated with anginal symptoms or dyspnea incurred on the left side.[11]

Although developmental variations in pulmonary structure, differences in pulmonary lymphatic and venous drainage, and pulmonary tissue resistance may explain the localization of pulmonary edema in certain instances, the position a patient assumes in bed should also be considered an important factor.[12]

Conclusion

A patient with unilateral pulmonary edema was found to have a preference for lying on her right side because of distressing symptoms when she lay on her left. No other cause for the localization of pulmonary edema could be identified. The position a patient assumes in bed may therefore be an important factor in the localization of intrapulmonary fluid.

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Famous Prefaces

Do but take care to express yourself in a plain, easy Manner, in well-chosen, significant, and decent Terms, and to give a harmonious Turn to your periods; study to explain your Thoughts, and set them in the truest light, laboring as much as possible not to leave them dark or intricate, but clear and intelligible.

— Cervantes — Preface to Don Quixote

A Practical Approach to the Patient with Seizures

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A SEIZURE especially a generalized grand mal attack, is one of the most dramatic symptoms of central nervous system dysfunction. Often a physician without a special interest in neurological disorders must treat a patient with seizures, perhaps on an emergency basis or as part of a family practice. This paper proposes to supplement the exhaustive details of the neurology textbooks with some practical advice.

A seizure is a symptom, not a disease. Any person is capable of having a seizure; thus not all patients with seizures have epilepsy. The term epilepsy, incidently, is no more specific than the term "crippled." It merely refers to patients with recurrent seizures and implies nothing about etiology. The chief problem facing the physician is to determine if the seizure is a symptom of a disease requiring specific therapy, or if it is a symptom of a chronic seizure disorder. Although the great majority of seizures occur in epileptics, many, if not most of the patients who have had one seizure or more, are not suffering from epilepsy. The epileptic carries an enormous social and legal burden. One should, therefore, hesitate before diagnosing any patient as an epileptic, reserving the term for those who have had more than one seizure not clearly related to a temporary condition.

The Emergency Treatment of Seizures

As a general rule a seizure, even the most severe grand mal attack, is a self-limited process. More than one general practitioner has learned to hitch up his horse slowly. By the time he arrived at the patient's house, the seizure was over. Repetitive seizures, however, especially repetitive grand mal attacks (so-called status epilepticus) are life-threatening. The patient must receive immediate treatment. The risks of status epilepticus are essentially those of respiratory embarrassment. There are many factors involved: obstruction, aspiration, prolonged apnea, and the increased energy demand and diffuse brain swelling accompanying repetitive seizures.

Stop the Seizures

In general, the safest and most effective means of stopping repetitive seizures is the slow intravenous administration of sodium amobarbital (Amytal®). Keep giving the drug until the seizure ends, but try to stop short of full anesthesia if possible. This form of treatment is, literally, the induction of general anesthesia with a short-acting barbiturate. Although amobarbital has no anticonvulsive action unrelated to its anesthetic effect (as phenobarbital has), it has the advantage of being short-acting and carries less risk of laryngospasm. Intravenous phenobarbital should be avoided because it takes 10 to 15 minutes to reach its full effect even with intravenous administration. As a result, overdosage is hard to avoid. Intramuscular phenobarbital in adequate dosage, at least

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100 mgm. for the average adult, is a very useful drug. Intravenous diphenylhydantoin (Dilantin®) carries a high degree of risk of central depression of respiratory and vasomotor control. Although it has been used successfully for the treatment of status epilepticus, unless one is expert, it is best to administer 100 mg. of Dilantin® intramuscularly. However, one should not rely solely on intramuscular Dilantin®. With intractable cases which do not respond to intravenous Amytal®, supplemented with intramuscular phenobarbital and Dilantin®, it may be necessary to use paraldehyde or to induce general anesthesia with ether.

Treat the Anesthetized Patient

When seizures are stopped in this manner, the physician must now deal with an anesthetized patient. It is absolutely essential that the airway be kept patent, that aspiration be avoided, and that artificial respiration be used if central depression of respiration has taken place. The blood pressure should be watched since the patient will frequently suffer impairment of cardiac and vasomotor function from the anesthetic, hypoxia and hypercapnia.†

Consider the possibility that the patient requires specific treatment for the cause of the seizure. One must always keep in mind the possibility that the seizure might have been caused by hypoglycemia or by anoxia secondary to impaired cardiorespiratory function.

Causative Factors

Temporary, Reversible Factors

Drug toxicity* or drug withdrawal** can cause seizures which need to be only temporarily controlled. Once the patient's metabolism has returned to normal, he will be free of the problem. Seizures accompanying high fever in children can also be included in this group.

Factors Requiring Specific Therapy

Acute infections (meningitis, encephalitis or brain abscess) are a frequent cause of seizures. Low-grade central nervous system infections such as syphilis, tuberculosis, and the fungal and parasitic infections may also produce seizures. Less common causes include hypovitaminosis (especially vitamins B-1 and B-6), hypothyroidism (in young children), hypocalcemia and hypoglycemia secondary to excessive insulin secretion. Electrolyte imbalance (in an extreme form, water intoxication) is a frequently overlooked cause.

A seizure may be a symptom arising from acute brain injury (trauma, subdural hematoma, intracerebral hemorrhage, subarachnoid hemorrhage, brain tumor) or acute cerebral vascular insufficiency (from stroke, myocardial infarction, cardiac arrhythmia or faint). The most common causes of seizures in elderly people are small strokes or other disturbances of cerebral circulation.

Epilepsy

There is a group of patients whose seizures are not amenable to specific medical or surgical therapy. Often we may know the cause of the seizure but not be in a position to do much about it. These patients, with chronic, repetitive seizures, make up the group that we commonly call "epileptics." They may be conveniently divided into two broad categories.

Symptomatic Seizures

These seizures are due to irritation by a lesion in the brain. Such irritation may be caused by scarring from an injury (accidental or neurosurgical), a brain tumor or a stroke. These changes are visible anatomically or pathologically. The most common cause of such seizures in the younger age group is injury suffered at birth. The temporal lobes, especially in the hippocampal† region, are notoriously susceptible to birth injury, and many of the large group of temporal lobe epileptics have seizures on this basis. Venous thrombosis will cause a scar leading to seizures and occurs especially in pregnant women.

The Clinical Forms of Symptomatic Seizures

a. Pure grand mal (generalized tonic-clonic seizures with immediate full loss of consciousness). A grand mal attack often occurs after any type of focal seizure.

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*e.g. Phenothiazines, antihistamines, too much insulin.

**e.g. Alcohol, barbiturates, meprobamate or Librium.®

†See Test Your Word Score Page 1491.

b. Grand mal seizures preceded by aura. The aura is actually a focal sensory seizure which spreads to a generalized seizure.

c. Focal motor seizures, limited to one limb or one side, may occur with preservation of consciousness.

d. Jacksonian seizures: focal motor seizures which start in one portion of the body and then spread to involve the rest of the side in a "march" along the motor cortex. These are quite rare but very dramatic.

e. Psychomotor seizures. These are more complex and bizarre than any other. The layman does not easily recognize them as seizures, although they can usually be recognized by the knowledgeable observer. Clouding of consciousness, incoherent speech, and amnesia for the episode are typical.

The motor manifestations range from the involuntary performance of partially coordinated movements to complex, highly coordinated activity which is recognized as involuntary only because it is so inappropriate to the situation. The patient may walk about, become combative, unbutton his clothes, expose himself, perhaps engage in aimless searching. If spoken to, it is apparent that he is not conscious of his environment. If he replies, the response is often irrelevant. Particularly helpful in making the diagnosis are the presence of lip smacking, chewing movements, and other minor motor phenomena more easily recognized as ictal. The attack may culminate in a grand mal seizure, sleep, or a prolonged period of confusion.

Many patients with psychomotor seizures also suffer from temporal lobe disorders, but one cannot speak of the two phenomena as synonymous. Not only must more knowledge of brain physiology be obtained before reaching this conclusion, but prolonged petit mal lapses are often indistinguishable from psychomotor seizures.

Cryptogenic Seizures

Idiopathic or cryptogenic epilepsy characterizes the other large group of epileptics. As the name indicates, we really don't know why these patients have seizures. There is

TABLE I

Drug	Indications	Total Daily Dosage	Side Effects	Precautions
Phenobarbital	Grand mal Focal motor Psychomotor	45-300 (average 90) mg. In infants & children, 2-4 mg/kg/day.	Somnolence	May produce hyperactivity in children. Dangerous to patients with porphyria (who may present with szs.)
Diphenylhydantoin (Dilantin®) (Phenobarbital and Dilantin are commonly used together.)	Grand mal Focal motor Psychomotor	200-600 mg/day. Infants & children, 2-6 mg/kg/day.	Gastric distress Acne Hirsutism Gum hypertrophy (control with good hygiene & massage) Fatigue Restlessness-children Incoordination-gait Nystagmus & diplopia	Permanent cerebellar damage may result from prolonged overdosage. Rash with fever usually disappears after dose is lowered. Can be increased later. Blood dyscrasia is rare.
Primidon (Mysoline®)	Psychomotor Grand mal	0.5-2 grams/day. Infants & children up to ½ adult dose.	Nausea & vomiting Dizziness & vertigo Somnolence Psychic disturbance	Start with very small dose and increase gradually.
Ethosuxamide (Zarontin®)	Petit mal	Children 0.25 G.-1 G/day. Adults 0.5-2 G/day. Start with low dose.	Rare. Anorexia, fatigue, psychic upset Dizziness	May increase frequency of grand mal if used alone; rarely causes leukopenia or pancytopenia.

a definite, although slight, hereditary tendency in many of these cases. Often one finds subclinical seizures or electroencephalographic abnormalities in the relatives of patients with idiopathic epilepsy. The seizures do not appear to be due to a scar on the cortex, but rather to a disturbance of upper brain-stem structures which have not been identified pathologically. Penfield and Jasper have coined the term '"centrencephalic epilepsy" for these patients who seem to suffer from a primary disturbance of consciousness as part of the seizure. These patients form the bulk of the group with idiopathic epilepsy. Grand mal seizures are the most common type. Some patients, especially young children, have petit mal staring spells, often with blinking of the eyes and chewing movements. These children may also have generalized grand mal seizures without aura. Rarer forms of seizures in these patients are akinetic drop attacks and myoclonic jerks.

The Treatment of Seizures

It is often difficult to decide if a seizure is symptomatic or idiopathic when the patient first consults you. All patients, therefore, are entitled to a careful evaluation. A good history, especially a clear description of the seizure, is of the utmost importance in evaluating the patient. A complete physical and neurological examination must be performed; and one should also check for the possibility of hypoglycemia, hypocalcemia, drug intoxication or withdrawal and syphilis. Most patients should receive an x-ray of the skull and a lumbar puncture. The electroencephalogram is also an exceedingly useful test, more helpful in determining the type and cause of seizure than in making the diagnosis as such. A certain number of patients, especially those with pure grand mal seizures, will have a normal electroencephalogram despite the best efforts of the examiner. Also, gross electroencephalographic abnormalities may be present in the absence of clinical seizures, especially in the relatives of centrencephalic epileptics. Contrast studies such as angiography and pneumoencephalography should be reserved, as a rule, for those patients with focal neurological signs.

Emotional Support

Before the doctor reaches for the prescription pad, the patient should be given a thorough explanation of his disease and a good deal of emotional support. It is often necessary to repeat this in a second visit and to allow the relatives to air their anxiety and obtain reassurance.

Precautionary Measures

It is wise to forbid driving (and airplane piloting!) until the seizures are under perfect control. Water sports are usually safe if seizures are infrequent and if the patient is closely accompanied by an expert swimmer. General measures such as adequate rest, a good diet, and counsel for and treatment of severe emotional upsets are very important. The adherence to a regular nonstressful regimen often spells the difference between complete and partial control of seizures. Diuretics for five days preceding menstruation are helpful in women whose seizures occur at that time. The patient should be encouraged to lead as normal a life as possible. More epileptics are handicapped by overly protective and anxious relatives than by uncontrolled seizures.

Anticonvulsants

Table 1 lists a few common anticonvulsants in order of decreasing safety; no attempt at an exhaustive list is attempted. Most patients can be handled with these four drugs either alone or in combination. When discontinuing any anticonvulsant, reduce the dose slowly over several weeks to avoid status epilepticus, which often occurs if drugs are suddenly withdrawn. As a rule, do not consider the withdrawal of anticonvulsants until the patient has been seizure-free for at least two years, and even then do so slowly over six to twelve months. Periodic blood counts should be performed. The more difficult problems should be referred to a neurologist.

Surgery

Surgery is indicated in those epileptics with (1) tumors or (2) severe seizures arising from a limited area of injury which have not been controlled after special handling with drugs. A very small percentage of patients meet these criteria.

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ANSWER TO WHAT'S YOUR DIAGNOSIS

(from page 1430)

The shadow (X-ray Figure 1) produced in the intravenous cholangiogram had the positioning of the gallbladder. A needle was inserted through the ribs and a purulent material encountered. Subsequent exploration into the peritoneal cavity relocated the abscess within the substance of the liver, having the length, breadth and approximate position of the x-ray shadow. It is speculated that the dye, when given intravenously, entered the abscess cavity, but when injected through the T-tube there was no communication (Figure 2).

The patient has made a complete and satisfactory recovery without recurrence of symptoms. Intravenous cholangiogram subsequently revealed no gallbladder shadow and the ring-like calcification was interpreted as being calcification of a vessel.

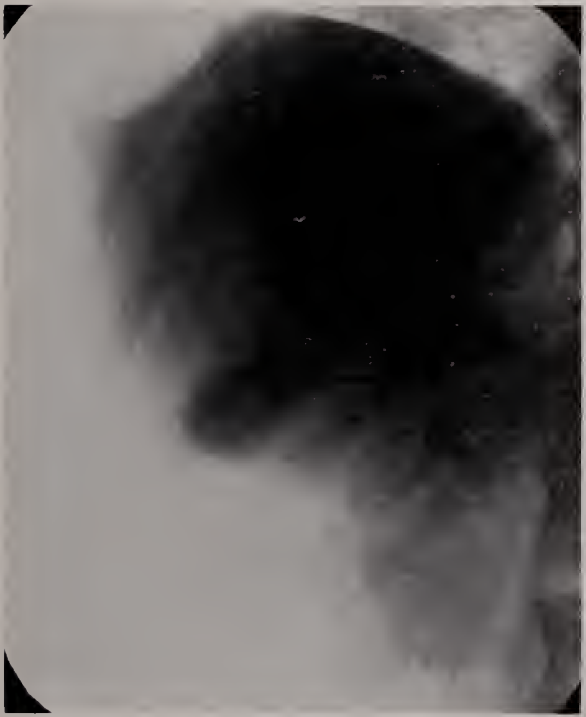

Fig. 1

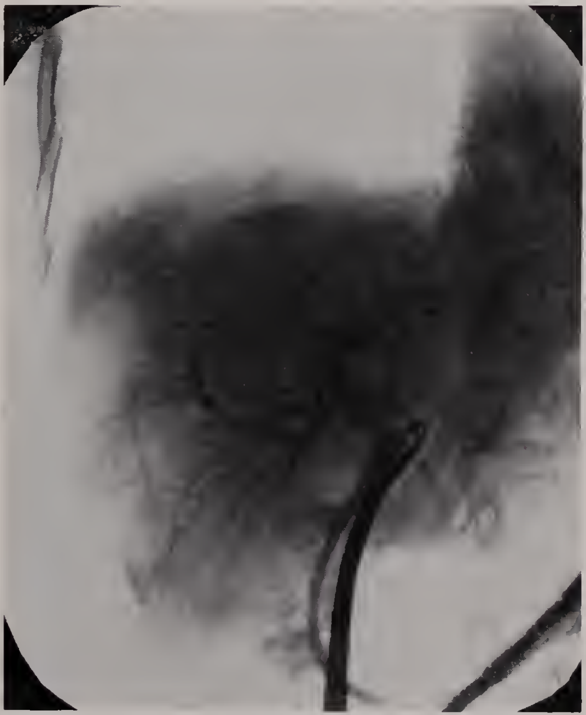

Fig. 2

There are parentheses in worry. — Balzac

Papillary Muscle Dysfunction

As EARLY as 1803 congestive heart failure and death resulting from rupture of a papillary muscle was known to occur, the mechanism of death being pulmonary edema secondary to acute severe mitral insufficiency.[1] By 1950 thirty-seven cases had been reported[2] and by 1963 this total had reached sixty-six.[3] No clear account could be found of mitral insufficiency and congestive heart failure as a result of dysfunction of a papillary muscle without rupture until Burch and associates described two cases in 1963.[4] In both cases the onset of the murmur was acute and followed myocardial infarction. Both cases ended in rapid death due to congestive heart failure, and both cases had the sudden onset of a murmur typical of mitral insufficiency as a clue to the diagnosis. Subsequently the same authors collected eleven additional cases and described clinical and electrocardiographic characteristics.[5,6]

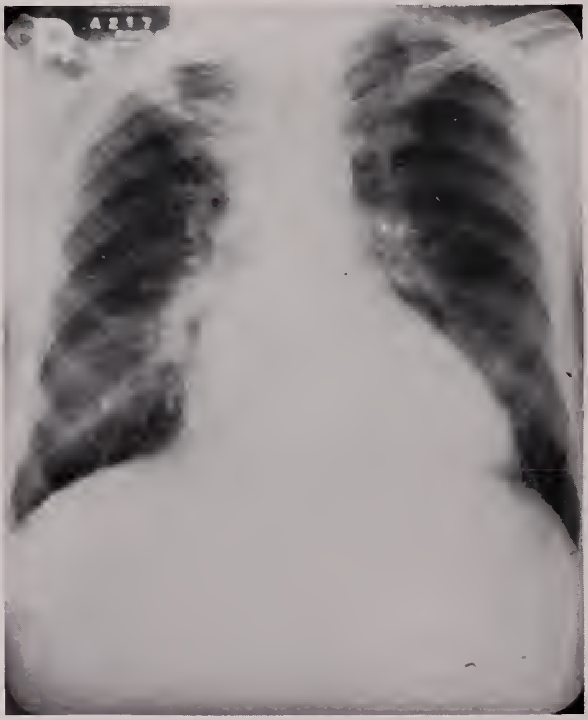
Fig. 1 — P-A chest roentgenogram demonstrating cardiomegaly and pulmonary venous congestion.

The frequency of papillary muscle infarction without rupture producing mitral regurgitation is emphasized by a subsequent report of fifteen additional cases.[7]

Because of the availability of corrective surgery for mitral valve deformities awareness of this entity is important.

The following case history deals with a patient without a history suggesting myocardial infarction. The patient was, in fact, undergoing evaluation for cardiac surgery because of severe mitral insufficiency thought to be of rheumatic origin at the time of his death.

Case Report

The patient was a 53-year-old white male at the time of his final Ancker Hospital admission in January, 1964. A review of his record revealed

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An Unrecognized Cause of Mitral Insufficiency

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periodic clinic visits and hospitalizations from 1934 to 1953 for sundry complaints. In 1953 he was seen in the orthopedic clinic for hip pain. An x-ray examination of both hips was normal. Over the next eight years he was essentially asymptomatic. In 1961 he was hospitalized for cellulitis of the face as well as for alcoholism. Cardiac findings were considered normal at that time.

In June, 1962, he was hospitalized with his first episode of congestive heart failure. There was no history of angina or chest pain. An electrocardiogram showed delay of intraventricular conduction but no evidence of myocardial infarct. An apical systolic murmur which radiated to the left axilla was present. He was treated with digitalis and diuretics and discharged with the diagnosis of congestive heart failure due to rheumatic heart disease with mitral insufficiency.

Over the next 17 months he had seven admissions for congestive heart failure, each bout becoming

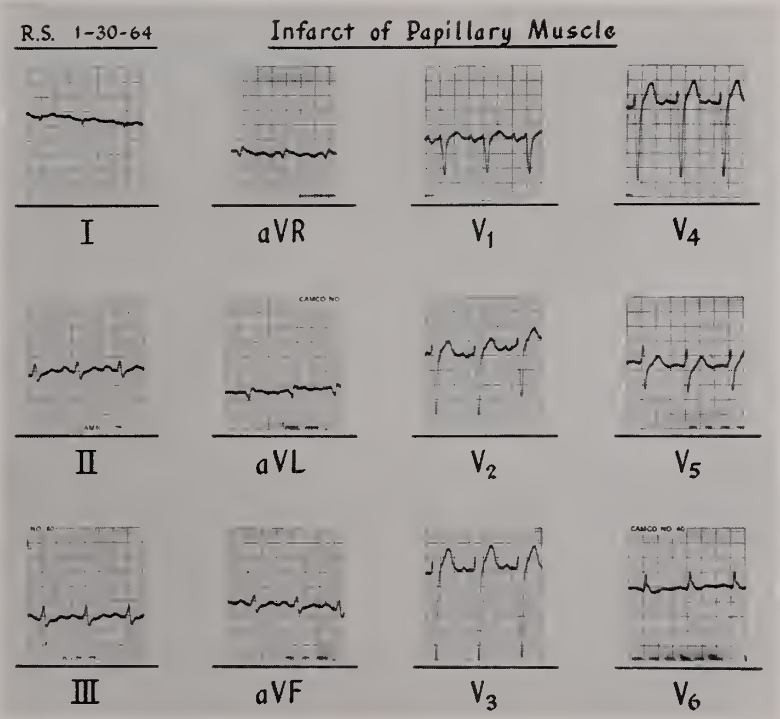

Fig. 2 — Electrocardiogram. A delay in intraventricular conduction is present. None of the described features of papillary muscle infarction are present.[6]

more severe. At no time could a history suggestive of myocardial infarction or angina pectoris be obtained. The murmur remained unchanged.

At the time of his last admission in January, 1964, his cardiac status was class IV. The chest roentgenogram at that time demonstrated marked cardiomegaly with dilatation of the left ventricle and congestive changes in the lungs (Figure 1). The electrocardiogram (Figure 2) revealed right axis deviation and ST-T wave changes of digitalis effect. The Q wave in AVL was thought to be due to the axis shift and electrical rotation of the heart. At that admission, mitral valve replacement was considered as definitive treatment for the mitral insufficiency. In preparation for surgery a left heart catheterization was performed. There was no demonstrable systolic gradient across the aortic valve. Most striking was an initial ventricular diastolic pressure of 20 mm. of mercury, and an end diastolic pressure of 37 mm. of mercury indicating a severe degree of left ventricular failure. Angiography was performed and demonstrated a large dilated left ventricle with severe regurgitation (4+) into the left atrium. This was best demonstrated in the lateral view (Figure 3). Aortography demonstrated no aortic insufficiency; the coronary arteries did not fill adequately for evaluation.

Intensive medical management of the left ventricular failure was instituted. On the third day following catheterization the patient suddenly developed shock and pulmonary edema. He denied pain. Ventricular tachycardia was noted on the electrocardiogram. In spite of vigorous therapy this arrhythmia progressed to ventricular fibrillation and the patient expired.

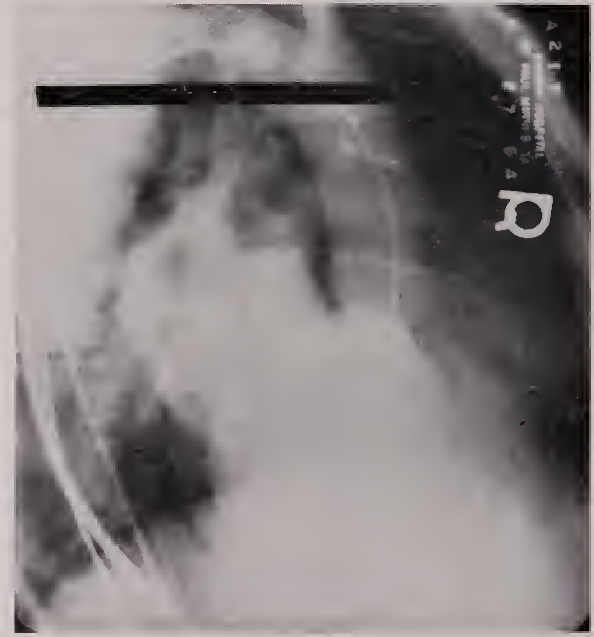

Fig. 3 — Left ventriculogram demonstrating the presence of contrast material in both the left ventricle and left atrium.

Autopsy Findings

At autopsy the heart weighed 755 grams. A very dilated and flabby left ventricle was noted. The coronary arteries showed grade 2 and focal grade 3 atherosclerotic changes. Right and left ventricular hypertrophy was present. The cut myocardium demonstrated a large area of subendocardial fibrosis in the anterior wall of the left ventricle. This extended laterally and inferiorly and involved both papillary muscles. These were noted to be very pale, thin, and atrophic (Figure 4). The cardiac valves and the chordae tendinae were normal.

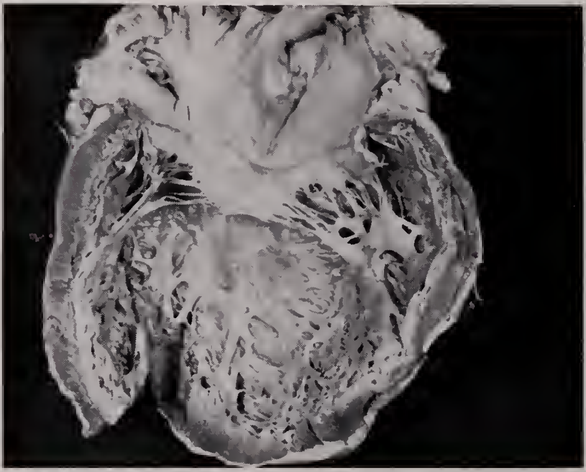

Fig. 4 — Gross pathologic specimen of the opened left ventricle. The papillary muscles are thinned and atrophic. There is no rupture.

Microscopic sections of the infarcted papillary muscles demonstrated a marked degree of fibrosis and disruption of the normal architecture (Figure 5). This was even more striking when compared with a section of normal papillary muscle which supplied the tricuspid valve (Figure 6). Collagen staining of the section of the infarcted muscle was also striking, the collagen making up a large part of the total muscle.

Discussion

For a clear understanding of how malfunction of the papillary muscles can allow severe mitral regurgitation, a brief resume of the normal function of the mitral valve apparatus including the papillary muscles is required.

Normal Function of the Papillary Muscles

In the left ventricle two papillary muscles are found. From each muscle head arise several chordae tendinae which insert into both leaflets of the mitral valve. Studies by Rushmer[8] have shown that the papillary muscles normally hold the valve leaflets within the ventricular chamber under tension. The free edges of the leaflets never pass higher than the atrioventricular ring. Following atrial systole the leaflets move together in light apposition, "floating" up under the influence of eddy currents produced by continued ventricular filling.[9] Normally, ventricular systole begins immediately thereafter, being initiated in the subendocardial area of the papillary muscles. Thus, they are the first area of the myocardium to contract. Their contraction causes the leaflets to be pulled firmly downward and together into a firmer degree of apposition. The myocardium now contracts in the phase of "isovolemic contraction," during which time the intraventricular pressure rises rapidly. This increase in pressure tends to balloon the mitral leaflets toward the atrium, but because of the firm anchor of the contracted papillary muscles, only the diaphragm of the leaflets moves upward, the free edges being held within the ventricular cavity. This ballooning effect causes a tight closure of the mitral valve.

Immediately following the isovolemic contraction phase is the phase of ventricular ejection. During this period pressures rise to the normal systolic level. This presents very high pressure per unit area to the leaflets, and certainly without the anchoring effect of the papillary muscles, the leaflets would evert into the atrium, allowing a severe degree of regurgitation.

Papillary Muscle Dysfunction

When papillary muscle dysfunction exists, the anchoring effect of their contraction is not present. However, with isovolemic contraction the intact chordae are able to prevent incompetency, and during production of the first heart sound the mitral valve is competent. During the phase of ventricular ejection the intraventricular pressure rises to the normal systolic level. Without papillary muscle contraction anchoring the mitral valve leaflets, insufficiency occurs and a murmur is produced. This murmur differs from the "pansystolic" regurgitant murmur usually associated with rheumatic mitral valve insufficiency in that there is a delay in onset

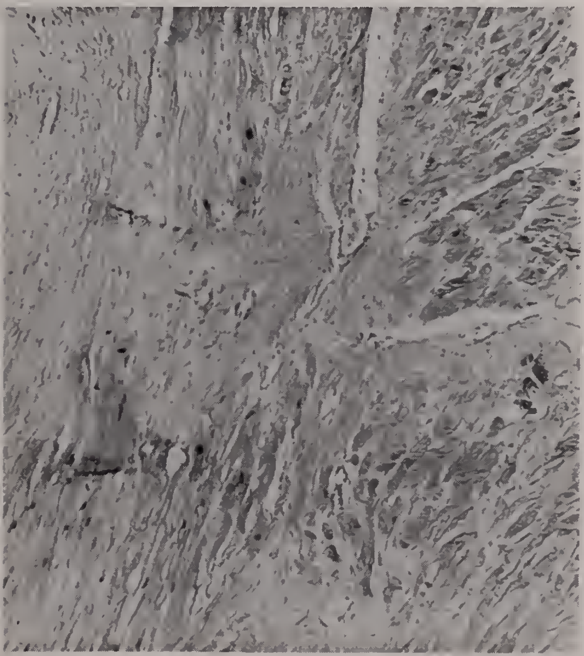

Fig. 5 — Microscopic section of the infarcted papillary muscle. Fibrous connective tissue predominates.

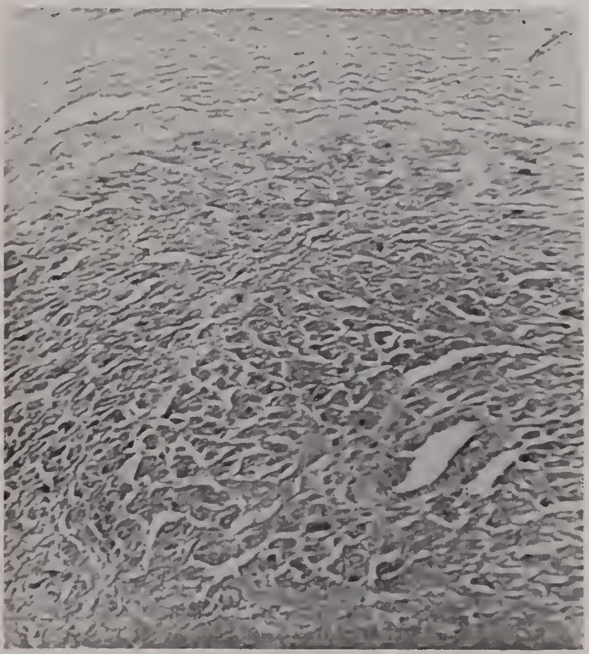

Fig. 6 — Microscopic section from right ventricular papillary muscle, demonstrating normal architecture.

from the first heart sound. The feature of delayed onset of this murmur, which is commonly of an "ejection" crescendo-decrescendo quality, is most important and serves to differentiate it from the murmurs of either rheumatic mitral insufficiency or rupture of papillary muscle wherein the murmurs are pansystolic.[4]

A more common example of dysfunction of the papillary muscles is seen in the case of premature ventricular beats. In such a case a ventricular systole is initiated before the leaflets have closed. Because the focus is ectopic, the papillary muscles are not the first areas to contract, and their effectiveness in closing the leaflets is lost. Thus, moderate degrees of insufficiency may occur.

In the case presented, dysfunction occurred as a result of loss of myocardial tissue in both papillary muscles. Because tissue was lost the atrophic muscles could no longer effectively hold the leaflets within the ventricular cavity; they could not contract effectively to initiate a firm apposition of the leaflets; and finally, as the ventricle contracted and as pressures rose, they could not act as anchors of the free edges of the leaflets, but allowed them to separate. Severe regurgitation through the mitral valve was the end result.

The adage that "Mitral insufficiency begets insufficiency" holds true in this case and undoubtedly later played a part in this patient, as the ventricle and the atrioventricular ring dilated. An already regurgitant valve became more regurgitant, and the cycle repeated itself. Death was the result.

Summary

A case is reported in which mitral insufficiency caused severe congestive heart failure. Due to lack of history suggesting coronary heart disease, a diagnosis of rheumatic valvular disease was made. Left heart catheterization demonstrated severe mitral insufficiency, a large dilated left ventricle, and pressures compatible with severe left ventricular failure. The patient expired and at autopsy was found to have coronary atherosclerosis and an old myocardial infarction with involvement of both papillary muscles. There was no papillary muscle rupture.

The function of the normal and diseased papillary muscles is discussed. Awareness of the entity of papillary muscle dysfunction due to infarction is important. Since corrective surgery for mitral valve abnormalities is increasing, the operative prognosis will depend not only on the nature of the deformity but also its cause.

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The secret of contentment is knowing how to enjoy what you have, and to be able to lose all desire for things beyond your reach. — Lin Yutang

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Character is much easier kept than recovered. — Thomas Paine

Bell's Palsy

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FACIAL PARALYSIS of sudden onset without demonstrable traumatic, neurogenic or otitic origin is termed "Bell's palsy." It has the potential for tragic and permanent disability. It has been mistakenly assumed for years that 80% of cases recovery spontaneously. This has encouraged the futile use of mild therapeutic exercises such as direct muscle stimulation in the thought that something harmless was being done to engage the patient through a period in which nothing useful could be done. This "head in sand" philosophy is untenable and bears discussion and rejection.

Eighty per cent of cases do not recover spontaneously if any discrimination is used in determining "recovery." Partial function and the bizarre character of facial synkinesis or "associated movement" are unacceptable levels of "recovery." Indeed, when discriminating standards are applied only 55% of Bell's palsy victims have satisfactory return of function. For the rest, permanent disability varies between troublesome and tragic as shown in Mathew's[1] series of 156 patients in whom results were graded as follows: (a) complete recovery; (b) incomplete grade 1 (incomplete recovery with no disability); (c) incomplete grade 2 (incomplete recovery with slight disability); (d) grade 3 (poor result). Mathews related the degree of recovery to the time of appearance of first movement (Table 1).

TABLE 1*
Degree of Recovery

Movement Observed	Complete Recovery	Grade 1	Grade 2	Grade 3	Total
4 weeks	74	6	18	4	102
4 to 8 weeks	0	1	10	7	18
8 to 12 weeks	0	0	4	7	11
12 or more weeks	0	0	1	13	14
Total	74	7	33	31	145

*From Mathews[1]

Diagnosis

All cases of facial paralysis see a physician as a matter of emergency once the enormity of the disability is apparent. Even those without associated pain see the disability as an acute disaster. Here is a time when medical piddling and procrastinating is costly, for adequate medical management can be valuable if immediately applied.

Careful otologic evaluation and neurologic study exposes specific disease in a few instances[2,3] of acute facial paralysis. Both are vital parts of the primary examination before the case can be categorized as an idiopathic or Bell's palsy. Pain in and about the ear of the involved side indicates a grave outlook for the Bell's palsy victim, but, where pain is a feature of onset, care must be used in examining for an herpetic eruption in the canal and conchal skin, else a geniculate herpes may be misdiagnosed as Bell's. In this regard, Cawthorne[4] has discussed the very real value of routinely performing the lacrimation test. This is simply performed by draping a filter paper strip from each lower conjunctival sulcus. The patient then is given ammonia to sniff. Equal lacrimation denotes pathology below the geniculate level as in Bell's palsy. The potential for erroneous diagnosis through incomplete study has been stressed by Walsh.[5]

In addition to excluding otitic or neurologic cause the first examination must establish the severity of nerve involvement through electrical testing.

Physiology

Under resting condition the membrane of a single nerve fiber is 20 to 100 times as permeable to potassium as it is to sodium. The membrane has a positive charge on the outer surface and a negative charge on its inner surface. However, this differential drops to zero or even reverses itself when the membrane becomes excited. This excitation may be physiologic or may occur by mechanical injury, or electrical stimulation, etc. This reversal of charge lasts but a half millisecond in larger nerve fibers before it returns to normal resting potential. This sequence of potential change is termed the "action potential." It causes an electrochemical impulse to be transmitted along the nerve fiber. The central core of the myelinated nerve fiber is the axon, and the surface of the axon is believed to be the actual conductive membrane. The axon is filled in its center with axoplasm — a viscid intracellular fluid. Surrounding the axon is a myelin sheath. Myelin is an excellent insulator and prevents almost all flow of ions through its substance. Approximately at each millimeter along the length of the axon, in a myelinated nerve fiber, the myelin sheath is interrupted at a "node of Ranvier." Because of the absence of myelin at this point ions can flow freely — indeed, the membrane here has been shown to be up to 500 times more permeable than the membrane of some unmyelinated nerve fibers. For this reason the electrical impulse generated by the action potential is conducted from node to node rather than continuously along the entire fiber. This process is called "saltatory conduction," and probably provides increased speed of nerve conduction and decreased metabolic requirement for the ion transfer process.

Larger nerve fibers generate greater numbers of electrical charges at each successive point along the membrane; therefore, the velocity of nerve conduction is almost directly proportional to the diameter of the nerve fiber.

A nerve trunk is made up of many fibers. The intensity of the impulse in a nerve trunk is controlled by spatial summation and temporal summation. Spatial summation refers to the number of individual fibers firing in a given nerve trunk. The action potentials of these fibers will summate at many motor end plates to activate many muscle units. Temporal summation relates to the number of impulses traveling along a single nerve fiber each second. This may, for example, be a hundred impulses per second. Muscle cannot react and recover this rapidly. Therefore, the impulses cumulate at the motor end plates during the muscle refractive period. This cumulation of impulses provides a greatly enhanced next stimulus. Normally nerve signals of different intensity vary in both spatial and temporal summation. In other words, the stronger the signal the greater the number of fibers involved and the greater the rate of impulse transmission by each fiber.

Experimental Nerve Destruction and Regeneration

When a peripheral nerve fiber is cut, the fiber distal to the cut will conduct impulses caused by electrical stimulation for two to three days. After that the entire nerve fiber peripheral to the section becomes inactive and the axons begin to degenerate. This is commonly termed "Wallerian degeneration." The neuronal body in the spinal cord undergoes changes termed, collectively, chromatolysis.*

Regeneration at the central stump of a single severed fiber is characterized by the elaboration of 10 to 100 searching fibers seeking any sheath in the peripheral end of the cut nerve. Once any sheath is found the searching fiber will follow it in peripheral growth at an average rate of a millimeter a day. Meanwhile the sheath cells enwrap the fiber and a new layer of insulating myelin is formed.[6] When many divided fibers are present the proximal searchers have no method of adopting the proper sheath and peripheral motor confusion is the end result (synkenesis or "associated movement").

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*See Test Your Word Score Page 1491.

Pathology

The presumed pathology in Bell's palsy[7,8] is acute, functional ischemia followed by capillary (endothelial) injury, transudation and constricting edema within the close confines of the tough nerve sheath inside the long bone canal (the greatest nerve length so confined in the entire body). The process of ischemia and secondary edematous constriction can result in: (1) neuropraxia (functional loss of conduction with axis cylinders anatomically intact) or (2) axonotmesis (loss of conduction due to necrosis of the axis cylinders); (3) a combination of both pathologies; or, (4) progression from neuropraxia to axonotmesis. By means of the nerve excitability test one can be differentiated from the other. This method of evaluating the status of the disordered nerve is cited by Richardson as superior to other modes.[9] He pointed out that nerve impulse velocity measurements were not readily applicable in facial palsy because the stimulus could not be applied proximal to the pathology. Application of stimulus peripheral to the pathology gave tardy and incomplete information with nerve impulse velocity measurements.

Similarly, Richardson cited evidence that strength-duration (I/T) curves depicting the threshold intensities of stimuli of various durations required to produce visible muscle contractions when applied over the area of motor nerve penetration of a muscle had no advantage over the simple nerve excitability test.

Electromyographic methods were noted to produce interesting information relative to degeneration and regeneration activities, but the information of greatest importance in the first days of the Bell's pathology lagged well behind that provided by the simple nerve excitability test.

Nerve Excitability Test

The nerve excitability test is simple and direct when performed with a proper instrument[10] applied at the zone of crossing of the main facial nerve trunk over the edge of the vertical mandibular ramus. The stimulator, used by the author, furnishes a square wave of negative polarity and duration of 600 microseconds with a repetition of 6 cycles per second. It automatically compensates for variations in the resistance of the circuit (and, therefore, in tissue resistance, i.e. anatomic variations) and thus delivers a current of determinable strength. The strength of current necessary to evoke response in a given individual is comparable from one side to the other. The acute palsy victim may show one of three findings: (1) identical muscular response to the same strength stimulus applied to the normal and the palsied nerves; (2) decreased (but present) response on the troubled side requiring greater stimulus (current); (3) absent response on the involved side. The prognostic as well as the diagnostic value of adequate nerve excitability test is shown in the relation between test response and eventual recovery (Table 2).

The fact that serial (daily) nerve testing is valuable in following initially unimpaired nerve excitability cases is demonstrated by Campbell[11] and by Laumans[12] and well illustrated in Table 3.

TABLE 2*
Nerve Excitability

Nerve Excitability	Cases	Full Recovery	Incomplete Recovery	
			Grade 2	Grade 3
Unimpaired	61	55 (90%)	4 (7%)	2 (3%)
Diminished	21	10 (48%)	9 (43%)	2 (9%)
Absent	35	7 (20%)	11 (31%)	17 (49%)

*From Richardson[9]

TABLE 3*
Eventual Recovery Compared with Nerve-Excitability Tests on 24 Patients Who Originally Had Unimpaired Excitability

	Cases	Full Recovery	Distortion on Movement	Distortion at rest and on Movement	Untraced
Partial Degeneration	15	10	3		2
Complete Degeneration	9	2	5	2	

*From Campbell[11]

Medical Management

Intelligent medical management of Bell's palsy is emergent. It should be started immediately upon recognition of the problem. Functional vascular alteration has been the focal objective of most recommended treatment. Vasodilation by physical therapeutic or pharmacologic methods has had proponents. Neural blocking therapy with intravenous procaine or cervical sympathetic block has favor with others. Endothelial repair with steroids has been recommended as has histamine-binding with heparin.

The authors feel that inpatient management with intravenous procaine-nicotinic acid infusion is a basis for good management. Its effectiveness is attested by the occasional neuropraxic case that has restoration of motor function during the infusion period. This invariably relapses to paresis within an hour or two of infusion termination, but the prognosis in such a case is invariably good and the evidence of restorative vascular effect is undeniable. The method of therapy as used follows:

A solution of 0.2% procaine hydrochloride is prepared in 5% dextrose (1 gm. of procaine hydrochloride in 500 cc. of 5% dextrose solution). To this solution is added ascorbic acid 1 gram and nicotinic acid 100 milligrams.

The rate of infusion is adjusted to produce a satisfactory reaction for both the nicotinic acid (warm flush) and the procaine (slight numbness, thick tongue, mild floating sensation). Extremes of these reactions should be avoided. Excess in one or the other should be balanced by increase or decrease in the nicotinic acid quantity in subsequent solutions.

A 250 cc. quantity of the above is given in one infusion period. It is repeated three or four times per day. No residual half-bottle is kept for longer than twelve hours.

The nurse (and the patient) are instructed to observe for facial movement during the latter part of each infusion period. This intravenous sequence is followed for seven days or until the nerve excitability test findings are stable for a seven day period.

In addition to the intravenous infusion 100 milligrams of hydrocortisone or its steroid equivalent are given orally in divided doses, each day, for a week or until the nerve excitability test findings are stable for that period of time.

The patient is instructed in uplifting facial massage and follows a ten-minute routine four to six times a day. He is also instructed in the care of the exposed cornea. Manual lid movement to moisten the cornea is practiced habitually through the day. The lid is manually closed at night and may be secured with a strip of transparent tape. The lower lid sag can be supported by an elevating strip of transparent tape lateral to the lateral canthus during the day. Protective eye glasses are advisable, particularly outdoors in the wind.

Surgical Management

It is of paramount importance that the patient with normal or decreased nerve conductivity be tested daily during the medical treatment period. Progressive decrease in responsiveness, even a week or more after onset, indicates a poor prognosis (Table 3). Therefore, progressive daily decrease in nerve conductivity is a clear-cut indication that surgical decompression of the nerve trunk be performed forthwith as an emergency effort to halt axis cylinder disruption. The loss of axis cylinders distal to the pathology, once established, makes full recovery impossible. A nerve trunk containing thousands of axis cylinders cannot recanalize this vast number of peripheral tubules accurately and completely. Partial permanent loss of muscular tone and strength can be less disastrous than the permanent "discord" of emotional expression from disorganized regeneration of the peripheral axons. Campbell's[11] figures show that of cases progressing to total degeneration subsequent to first examination only 20% made a satisfactory recovery.

For the nerve in which neuropraxic elements with axis continuity are present in useful numbers the spontaneous and medical resolution of vascular pathology should find those elements improving in nerve test response within weeks. Where no nerve excitability is present after two weeks it can be assumed that the pathologic state within the facial canal is of an unremitting and severe type.

For the patient exhibiting absent electrical response at first nerve excitability test, the prognosis for full recovery is poor. The axis cylinders are already disrupted. The long, fumbling, and disorderly recanalization of the thousands of distal sheaths by the groping, amoeba-like proximal stumps must go forward until the motor end plates are reached.

Laumans[13] has demonstrated that where complete degeneration has occurred full recovery is out of the question. Jongkees[14] points to the fact that such patients constitute a select and tragic classification and have a uniformly poor outlook for good recovery — a sharp contrast to the cheery expectancy of the neuropraxic case. It is Jongkee's feeling that decompression surgery should be performed immediately since in this selected group further conservative management has proven almost 100% unsatisfactory.

There is sound evidence from many sources that resolution of the pathology can be expedited with skilled microsurgical decompression of the nerve from the middle ear to the stylomastoid exit. This is urged when nerve excitability is absent after two weeks of observation and adequate medical management. Long delay can result in partial or total replacement of the disintegrated fibers by fibrous tissue.[15-17]

Summary

1. Bell's palsy is an acute medical emergency.

2. Careful otologic and neurologic study is necessary since the diagnosis is made by exclusion of other cause for the acute palsy.

3. Immediate (first day) evaluation of the state of the nerve by the relatively simple nerve excitability test must be followed by daily retest to follow the progression of the pathology.

4. Aggressive inpatient medical management is outlined.

5. When severe pathology persists or progresses in spite of treatment a tragic prognosis can be improved through surgical decompression of the nerve.

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The distance is nothing; it is only the first step that costs. — Mme. Du Deffand

Man is a piece of the universe made alive. — Emerson

PEUTZ-JEGHERS SYNDROME

This syndrome is characterized by polyposis of the mucosa of the small intestine and unusual skin and mucosa pigmentation. The disorder is familial in fifty per cent of the cases inherited as a simple mendelian dominant. It occurs in all age groups and in both sexes.

The clinical manifestations consist of colicky abdominal pains, gastro-intestinal bleeding and, in some instances, episodes of invagination with intestinal obstruction, especially in children.

The areas of cutaneous pigmentation consist of dark brown melanin deposits, appearing at one to five millimeter round, oval or stippled areas on the lips, the skin of the face and digits, the nasal area, around the eyes and mouth and occasionally on the genital or rectal mucosa.

The polyps are demonstrated roentgenologically, most commonly located in the small intestine, but can also be found in the stomach, large intestine, and rectum. Low-grade malignant degeneration has been found to occur in twenty per cent of reported cases.

Resection of the involved area of intestine is indicated as a prophylactic measure, and becomes imperative when severe bleeding or obstruction develop.

— Durham, Robert H. — Encyclopedia of Medical Syndromes,
Hoeber Medical Division, Harper and Row, New York

The Papyrus Ebers

Those about to study Medicine, and the younger Physicians, should light their torches at the fires of the Ancients. — Rokitansky

The Ebers Papyrus is an excellently preserved Egyptian scroll 12 inches wide and 68 feet long, written in 1500 B.C. It consolidates into a unitary document the record of Egypt's medical remedies from 3400 B.C. up to the time of its transcription from the original hieroglyphic form into more legible hieratics.* The papyrus comprises Book 40 in the totality of 110 Egyptian books known as the Hermetic Books, purportedly containing the sum of all human knowledge, and is one of six dealing with ancient medicine — antedating even the Greek contributions to medical science.

The Egyptologist so fortunate as to secure the papyrus from a native Egyptian was Georg Ebers (1837-1898), who took his precious find to the University of Leipzig where it now reposes. The abstruse, archaic, and somewhat controversial document was ably translated into German by D. H. Joachim, who said: "It surpasses in importance all other medical papyri in the richness of its contents and its completeness and perfection. It is the largest, most beautifully written, and the best preserved of all the medical papyri."** Joachim's German version was later translated into English by Cyril Bryan, whose work is highly commendable not only for its exposition of the text, but also for the warm, human insight it injects. The medical section of the Hermetic Books consists of Book 37 on Anatomy, Book 38 on Diseases, Book 39 on Surgery, Book 40 on Remedies, Book 41 on Diseases of the Eye, and Book 42 on Diseases of Women. Subsequent issues of MINNESOTA MEDICINE will explore the Ebers Papyrus in more detail.

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*Hieratics: a cursive script adapted from hieroglyphics.

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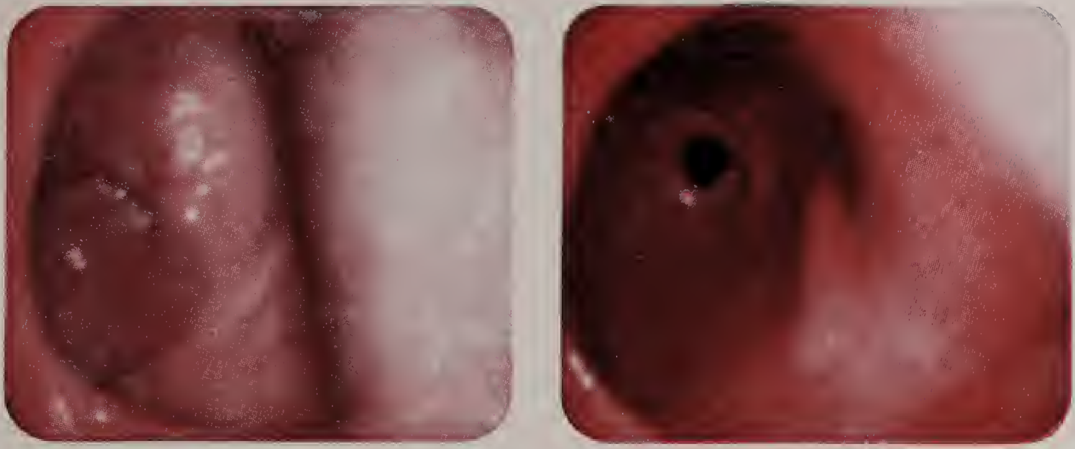

Intragastric photography studies[1]

A/ E. B., male, age 48. Normal antral contraction. Pyloric opening is not seen. It is difficult to differentiate a deep prepyloric contraction from a "pyloric fleurette" or true pylorus.

B/ Same subject after 6 mg. of propantheline bromide intravenously; antral contractions ceased. The pyloric orifice remained open and was easily identified. Better visualization of the antrum was also obtained.

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(propantheline bromide)

Pro-Banthīne is so effective in anticholinergic action that it may be employed in visualizing the entire pyloric region.

In addition to the intragastric photographs, cinegastroscopic studies[2] have demonstrated graphically not only its effectiveness but the superiority of Pro-Banthīne over belladonna alkaloids.

Pro-Banthīne produced complete cessation of gastric, antral and pyloric motor activity with a dose of 6 mg. intravenously. This is approximately one-third the usual oral dose of 15 mg.

Atropine at full normal dosages did not produce such cessation. It required double the usual oral dose of atropine, 0.8 mg. intravenously, to duplicate the aperistaltic action of Pro-Banthīne. This dose of atropine produced pronounced discomfort and tachycardia with ventricular rates as high as 150 per minute.

It is this pharmacologic superiority of Pro-Banthīne which has made it the most widely prescribed anticholinergic in such conditions as peptic ulcer, functional hypermotility, irritable colon, pylorospasm and biliary dyskinesia.

Dosage—The maximal tolerated dosage is usually the most effective. For most *adult* patients this will be four to six 15 mg. tablets daily in divided doses. In severe conditions as many as two tablets four to six times daily. Pro-Banthīne (brand of propantheline bromide) is supplied as tablets of 15 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type ampuls of 30 mg.

Side Effects and Contraindications—Urinary hesitancy, xerostomia, mydriasis and, theoretically, a curare-like action may occur. The drug is contraindicated in patients with glaucoma or severe cardiac disease.

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Editorials

A Medical Internship under Dr. Arthur B. Ancker*

1904-1905

WITH THE NEW Ancker — City and County Hospital rising up majestically on University and Jackson Streets in St. Paul, it calls attention to the great contrast between that building with its great teaching staff and the old City and County Hospital overlooking the Mississippi River on West Seventh Street when Dr. Arthur B. Ancker was running the whole show.

The City-County Hospital and Dr. Ancker were so closely related that one can not speak about one without the other. He was the hospital! Dr. Ancker's personality penetrated the whole institution from the kitchen to the front office.

He and his staff had selected seven of us, nice green students fresh out of medical school, for that class of interns for 1904-05. They were Doctors Carl A. Larson, George Dittman, Tobias Birnberg, William F. Frost, Edward M. Mauer, A. G. Schulze and myself. We all had our M. D. degrees, for at that time it was not necessary to have an internship to get the degree or to be able to practice. This was most important to all of us as I will point out later.

The hospital worked on the rotating system just as they do today but it must be remembered that this was 1904 — sixty years ago — and even though we had the same services, we were offered nowhere near the depth of instruction that is common now. There just wasn't the medical knowledge then. Pathology was very simple by today's standards. We could count red and white blood cells, examine urine and we did smears for staph and strep. Before my year was over we started to differentiate between the mononuclears and the polynuclears. But most of the time we simply counted white cells and paid no attention to the differential count. We did a diazo urinary test and a Widal blood test for Typhoid Fever but when it came to bacteriological work, we sent our diphtheria cultures to the City Health Department at City Hall. No routine autopsies at all. If we had an autopsy, it was to look at something rare or unusual. Autopsies were simply for gross pathology, for little microscopical work was done. That was the extent of our laboratory pathology.

X-ray equipment was of the crudest form and a far cry from the most sensitive and advanced equipment that is being installed for the radiology department in the new hospital. Eight years before I arrived at the hospital the first successful X-ray picture was taken. Professor Fred S. Jones of the

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*An excerpt from the biography of Harvey Ogden Skinner, M.D., as written by Lillian Thomas Smiley.
St. Paul Pioneer Press, October 3, 1965.

Some people get away from colds and sinusitis
by getting away from frigid weather

. . . but if your patient can't get away, relieve sneezing, running nose, and congestion of colds and sinusitis all day or all night with one

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Physics department of the University of Minnesota produced the picture and Dr. Millard performed the operation: the removal of a bullet from a man's leg. The newspapers for that day reported that the doctor was "aided by the photograph (and he) cut directly to the spot where the bullet was shown in the X ray." According to the newspaper, this was the first operation with the help of X ray in the northwest.

The excellent teaching staff made up for the lack of medical knowledge and modern equipment. We had giants of medicine that made our instruction at City and County Hospital one of the outstanding teaching hospitals in the nation and certainly the best in the west.

One of the great opportunities of a lifetime was to train under Dr. A. J. Gillette, orthopedic surgeon, sometimes referred to as the 'Dr. Lorenz' of America; Dr. Justice O'hage, surgeon, who took out the first gall bladder in the United States at St. Joseph's Hospital in St. Paul — the 10th recorded cholecystectomy in the world. Doctors E. J. Abbott, J. A. Rothrock, Walter R. Ramsey and Longstreet Taylor, all come to mind as the medical giants of that day, but there were many, many more.

These men were appointed to the hospital staff in 1892, the first time Dr. Ancker had a full hospital faculty that gave their time and knowledge without compensation. Five years before the first appointed staff, records show the first intern and the only one for that year. His name was Dr. F. H. Holland and Dr. Ancker was his only teacher.

In 1896 Homeopathic doctors were invited to join the faculty staff but their invitation came under extreme opposition from Dr. Ancker, major-domo of the hospital. Dr. Ancker did not want to recognize homeopaths because of their fundamentalist faction, but he would recognize the liberal group. Again, it was the same kind of fight that went on at Hahnemann College in Chicago as late as 1920, which led to its decline and closure. Also, as he was an allopath, he had doubts about the two groups working side by side in the hospital. There was a running battle between Dr. Ancker and the more out-spoken city Homeopaths for more than two years. The newspapers were full of the controversy. The Homeopathic doctors even threated court action, but only because Dr. Ancker was so adamant and dictatorial in managing the City and County Hospital. Dr. B. H. Ogden and Dr. Henry Hutchinson were of the liberal group of Homeopaths and much more open-minded than the fundamentalists, who clung to believing absolutely in "symptom matching only." But Dr. Hutchinson in his quiet, intelligent way finally brought Dr. Ancker around to an agreement.

Even these illustrious and forth-right staff doctors knew it was Dr. Ancker's Hospital. Dr. Ancker saw to that himself; that anyone in and around the institution worked within *his* rules or they didn't. It was as simple as that. But there was a reason for this.

In 1872, ten years before Dr. Ancker set foot in Minnesota, the Ramsey County Board of Control bought from Dr. Jacob Stewart, later mayor of St. Paul, an old stone mansion and its grounds for hospital purposes. This was the same property where the present 'old' Ancker Hospital stands just off West Seventh Street. The Board got the property for a 'song,' something around $20,000, according to Dr. Ancker's records.

Dr. Ancker had received his medical degree from the Medical College of Ohio in Cincinnati and had been in St. Paul only a year when he was named by the Board to be superintendent of the City and County Hospital. The Board of Control saw in Dr. Ancker just the man they needed to start a hospital. Therein lies the devotion Dr. Ancker had for his hospital: he got it started; he worried with it and he alone was responsible for its growth.

The 'hospital' consisted of ten rooms with two bathrooms and a barn out in back. Dr. Ancker's contribution to the institution was a few miscellaneous instruments and a prescription pad, all of which he could carry in his pockets. He said at the time, he "was the whole institution." He had no staff, no nurses, no training school, nothing. The interior equipment included 27 stoves and a collection of kerosene lamps; no electricity,

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gas or sewage disposal and they carried their water in with buckets from a well on the property. In the beginning, he had one woman working for him who scrubbed the floors and cooked the food. The barn out back was used, not only for Dr. Ancker's horse but also, the first floor was the morgue or better known as the 'dead house.' Upstairs, the old hay loft was used for isolating contagious patients. It may have been no consolation for a delirious patient, racked with fever, to be in with the dead and one live horse, but Dr. Ancker literally had no other place for them.

Dr. Ancker saw all the patients personally and if all the beds were full, his rounds would include forty people. If he ran into difficulty, he sometimes would send for either Dr. Charles A. Wheaton, Dr. Everett G. Abbott or Dr. Edward C. Spencer, then well-known practicing physicians in St. Paul. But most of the time he did everything himself. Dr. Ancker recalls that in the early days he did all the police surgery. St. Paul was still a rough and ready river town in the 1880's and early documents show he was busy with casualties from that element.

He had no operating room as we know it; he would just throw a screen across the end of one of the larger rooms and go to work behind that. It has been said that the stronger patients would be called in at night to hold the kerosene lamps over the field of operation.

Dr. Ancker was a czar who flew often and regularly into violent rages. As our class of interns would say, "Dr. Ancker is having a hemorrhage of green paint," when he went into one of his outbursts. Many times I have heard him yell, "I'll be in charge here, not the staff!"

During the time when I was under his direct rule, he was around fifty years of age, an alert, wiry, restless man. He was of light build with small hands and his features were plump. He had had his left shoulder joint incised for tuberculosis, so he had a little difficulty getting his overcoat on and he always walked with that arm hooked to his side, but otherwise it didn't seem to bother him or inconvenience him in any way.

His demeanor was such as to not tolerate any insubordination. He would storm into a room and reach way up under a bed and if finding the least amount of dust, would scream, "this place is filthy — this place isn't fit for cattle." Then he would look around and the first nurse he saw caught it. When anything occurred not to his liking, he went into his rages. It didn't make any difference who was responsible, the first person he saw — it might be a nurse at the end of the hall, or a steam-fitter fixing a pipe — the first one caught "the hemorrhage of green paint."

Dr. Ancker was everywhere at once, it seemed, for he would show up in the most unexpected places, at the least expected time. And woe be the man who was in the room if anything went wrong. He always called the interns, 'Mr.,' not 'Doctor' and I have heard him yell "Mr. So and So, I will have you to understand these are human beings that you are taking care of."

No doubt about it, Dr. Ancker ran an extremely efficient hospital. Everyone lived in terror of his temper explosions, but everything was in perfect order, from the cleanest of floors to every medical report written up and signed. If an intern did get behind in writing up his surgical notes, again the storm would descend around his head with, "do you want this hospital to go broke with law-suits, etc., etc."

Except for his explosive temperament, he was a very fine man. He had keen sense of values, high ideals, a good education and his decisions, which he enforced with his iron will, were sound. Even though his enforcement was with unnecessary severity, he saw to it that 'his hospital' was the best and above standard.

In regard to my personal experience with him I had no real trouble. I was called into his office only once and for some reason he didn't "hemorrhage his green paint" on me. He treated me like a thoughtless schoolboy and he was playing the part of a chastising father.

There was one explosive event where I was involved, but only on the fringe of the trouble. This happened near the end of my

Continued

Anatomy of
Low Back Pain #1
the sedentary life
is often the seat of
low back pain

The human spine is not engineered
prolonged sitting at desks, pianos, t
writers and drafting boards. The stres
set up by the heavy, forward-tilted h
and trunk, balanced precariously or
insufficient base, result in strain of
dorsal musculature, particularly at
low lumbar level.

*The unusual muscle-relaxant and a
gesic properties of 'Soma'* make it es
cially useful in the treatment of low b
sprains and strains. 'Soma' is wi
prescribed ☐ **to relieve pain** ☐ **to r
muscles** ☐ **to restore mobility.**

Indications: 'Soma' is useful for managemе
muscle spasm, pain, and stiffness in a varie
inflammatory, traumatic, and degenerative mu
loskeletal conditions. It also may act to norm
motor activity in certain neurologic disturba

Contraindications: Allergic or idiosyncratic
tions to carisoprodol.

Precautions: 'Soma', like other central ner
system depressants, should be used with ca
in patients with known propensity for taking
cessive quantities of drugs and in patients
known sensitivity to compounds of similar ch
cal structure, e.g., meprobamate.

Side Effects: The only side effect reported with
frequency is sleepiness, usually on higher
recommended doses. An occasional patient
not tolerate carisoprodol because of an indivi
reaction, such as a sensation of weakness.
rarely observed reactions have included dizzi
ataxia, tremor, agitation, irritability, headache
crease in eosinophil count, flushing of face,
gastrointestinal symptoms.

One instance each of pancytopenia and le
penia, occurring when carisoprodol was ad
istered with other drugs, has been reported, a
an instance of fixed drug eruption with carisop
and subsequent cross reaction to meprobar
Rare allergic reactions, usually mild, have incl
one case each of anaphylactoid reaction with
shock and angioneurotic edema with respir
difficulty, both reversed with appropriate the
In cases of allergic or hypersensitivity react
carisoprodol should be discontinued and appr
ate therapy initiated. Suicidal attempts may
duce coma and/or mild shock and respira
depression.

Dosage: Usual adult dose is one 350 mg. t
three times daily and at bedtime.

Supplied: Two Strengths: 350 mg. white ta
and 250 mg. orange, two-piece capsules.

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**for the relief
of low back
sprains and strai**

**SOM
(CARISOPRODO**

Wallace Laboratories, Cranbury,

internship, in fact two weeks before my service was to be completed. On May 18th, 1905, The St. Paul Dispatch ran big headlines on the front page that read, "Striking Physicians at City Hospital — Interns are Discharged." Here is the story of that blaring statement and certainly more of the truth than the headlines conveyed.

Dr. William F. Frost, one of the interns in my class, didn't report directly to Dr. Ancker about the negligence of a nurse. On his own, Dr. Frost just took care of the misconduct of the nurse and then forgot about the incident. About two months later, Dr. Ancker found out about it and hit the roof. He said the incident had been reported outside the hospital without his knowledge and besides the misconduct of the nurse should have been reported to the superintendent of nurses *and* to him for proper discipline. The matter was so trivial and inconsequential that some of our members didn't even know anything about it, let alone Dr. Ancker. But he was boss and because he would not tolerate any looseness in control, Dr. Ancker fired Dr. Frost.

Dr. Frost's position was that the incident was two months old; he had not talked about it outside of the hospital and no serious damage had been done. He didn't think it necessary to take such a small thing to Dr. Ancker. He informed Dr. Ancker that he would not resign, for he was not guilty of any offense, either to the hospital or Dr. Ancker. He felt his suspension so unjust that he took his case to the Ramsey County Board of Control, over the head of Dr. Ancker.

Before Dr. Frost gave the Board his side of the question, the Board informed him no charge had been made against him and he could speak freely. Dr. Ancker was in attendance at this meeting. At the end of the hearing, he was told again no charge had been placed against him and he was to continue his work until the matter was settled, which meant that the Board would take it all up at a later meeting.

The following morning in the midst of an operation, Dr. Ancker demanded that Dr. Frost leave the operating room at once. Again, Dr. Ancker's temper showed up at the unexpected time. Also, this was the second time Dr. Ancker had suspended him without charge. When the rest of us heard about it, we all felt it was unjust and uncalled for discipline and that Dr. Ancker had gone too far. The other interns thought the only thing to do was to walk out. It was a nasty mess and when the newspapers got hold of the story they really played it up. It wasn't really a strike, for no one really intended to walk out, just go as a body to Dr. Ancker and issue a formal protest. We were only standing up for Dr. Frost.

My part in the matter was never clearly understood and this is probably my first chance to explain it all. When I went into City and County Hospital, I was the underdog, because I was a Homeopath. And I really didn't know just what part I should take in this matter. The only thing I could see to do was to consult Dr. Ogden and Dr. Hutchinson, the two top men on the City and County Hospital Staff and also Homeopathic doctors. After their discussion they advised me to stand by the interns, if I thought they would do the same for me in a similar case. There was no question in my mind that my fellow interns would do the same for me. They agreed with me and said, "go ahead." So I went out, not on my own hook but with considered advice from the two biggest men on the staff. Whether they reasoned that we were so close to the end of our internship and it didn't matter, or that maybe this would show Dr. Ancker he couldn't always get away with acting the part of an unreasonable dictator, I don't know. But I do know they didn't think it was wrong on my part.

Dr. Ancker stood his ground and we all left two weeks early. There wasn't a hitch in services for the sick and I doubt that a patient was even aware we were gone. There was no hardship for the hospital for Dr. Ancker just called the next class of interns in two weeks early. But the newspapers slanted their story that we were ungrateful kids and we had no honor.

We all had our M.D. degrees when we came for our internship and as I said before we didn't need the internship to practice.

The whole incident made me ashamed, so

Continued

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It stands to reason. They all go through the same training; they all have to pass the same tests; they all have to measure up to the same standards. Therefore, all registered nurses are alike.

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You might also say that all registered nurses aren’t alike, either.

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later I wrote a letter of apology to Dr. Ancker. I didn't want to have him think too hard of me. While I had gone out with the fellows, I had not done it in a fit of temper, but with considered judgment of highly respected physicians in St. Paul. Nothing ever came of it, but I wanted to set the record straight between Dr. Ancker and myself.

The marriage of City and County Hospital and Dr. Ancker went on and on for a total of forty years. When he died on May 15th, 1923, he was eulogized in every twin city newspaper and many of the national medical journals. He had built the City and County Hospital into a top respected position, recognized by medical schools as an outstanding teaching hospital. He was considered an architect of hospitals from his personal experience and from the many articles and speeches he had made about building such institutions. He had been a president of the American Hospital Association and at the time of his death he was on the editorial board of *Hospital Management.*

He literally died "in the harness," for he was making rounds in the hospital, and the story goes he still was in his usual form when he exploded in the surgeon's washroom because he thought the surgical interns were not getting their hands clean enough for surgery. He returned to his office to prepare a talk for the local medical society when he collapsed and died of a coronary attack.

Shortly after, the City and County Hospital name was changed to Ancker Hospital in his honor and Ancker Hospital it has been known for the past forty years.

Lillian T. Smiley*
Minneapolis, Minnesota

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Pediatrics: Yesterday, Today, and Tomorrow

The Emergence of Chronic Diseases as Management Problems of Childhood

Pediatrics Past

THE DEVELOPMENT of present medical knowledge is the product of the translation of basic research findings into practical application as well as the result of stimulation for incisive investigations prompted by astute clinicians.

A bidirectional flow of concepts and ideas from the research laboratory to the patient and from the bedside to the investigator has produced vast strides in man's attempts to eradicate disease. The discerning observations of Jenner,[1] and of Chain and co-workers,[2] and the application of the basic viral culture techniques of Enders, Weller, and Robbins,[3] Salk,[4] Sabin,[5] and others are pertinent examples of such effective translations.

Some of the diagnostic and therapeutic challenges of a generation ago are now among the roundsmanship repertoire of the junior medical student. However, as a result of recent advances in medicine, it is not unusual to find a student, intern, or resident who has never seen a diphtheritic membrane or heard the characteristic "Whoop" of pertussis. The bedside vigil with the bulbar poliomyelitis patient is fortunately no longer the virtually helpless task it was slightly more than a decade ago. Bacterial pneumonia, otitis media, diarrhea, and venereal disease no longer threaten the infant as they did a generation past. Meningitis, treacherous though it remains, is no longer associated with the almost universal fatality of the preantibiotic era. Acute infectious diseases, so serious in the age of our own childhood, now yield in large measure to a variety of antimicrobial agents. The premature, or immature infant, having escaped the iatrogenic insults of hyperoxygenation, vitamin K, and sulfa drugs, now faces a greater chance of survival, with subsequent normal growth and development, than ever before. Formula manipulations have been responsible for serious metabolic disturbances in infants.

Continued

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These tragic good intentions from the past should focus our attention on Hippocrates' dictum, "do no harm," and serve to continually warn us that the "remedy" may be worse than the disease.* The thalidomide tragedy is a poignant example of this error; and today there is some evidence to suggest that perhaps routine vaccination for smallpox should be discontinued in the United States.[6]

Thus, pediatrics yesterday was characterized by a high mortality rate from acute infectious diseases, frequent morbidity with prematurity, vitamin deficiencies, and the lack of modern surgical techniques. Effective vaccines, potent antimicrobial agents, a virtual vitamin "fall out," and corrective surgery have significantly reduced these problems. The multidisciplined team approach composed of surgeons, anesthesiologists, electronic engineers, physiologists, biochemists, and scientific instrument technicians have made possible cardiopulmonary, ophthalmologic, and neurosurgical procedures which were considered impossible a decade or two ago. Today a wide variety of congenital defects of infancy are amenable to corrective surgery. Continued application of basic virological techniques provides the means of rendering extinct rubeola and, hopefully, other viral diseases. Human serum or gamma globulin, hyperimmune for various diseases, including tetanus and possibly rabies, promises to eliminate the necessity for having to choose between the lesser of two evils when, for example, the physician is faced with the choice of the risk of tetanus or the high frequency of serum sickness.

Pediatrics Present

Improved prenatal care and obstetrical techniques have contributed much to the armamentarium required for the accomplishment of gestation in many mothers. Pediatrics today, however, faces a new kind of challenge — accidental death and poisoning. Again, attempts to be "helpful," i.e., inviting and attractive products and packaging, have resulted in the ingestion of toxic household agents such as floor wax and cleaning fluids. Our pharmaceutical colleagues now supply us with the most appealing and palatable medicines ever devised — a far cry indeed from the days of sulfur and molasses. With such delicious products, is it any wonder then that "flavored baby aspirin" repeatedly occupies such a high rating on the list of poisons ingested by children?

Additional hazards which face the child of today are related to our changing sociologic structure. The maternal deprivation syndrome, the fatherless child, and the battered child pose difficulties in understanding and complexities in management sufficient to require a modern Solomon for solution. Certain it is that the pediatrician of today must assume a more "social" role as a member of the physician-patient-parent-school group interested in good health for all children.

The Complete Pediatrician

Pediatrics today requires an even greater utilization of the basic biochemistry and physiology so often committed to oblivion by the sophomore medical student following final examination. Successful management of disturbances in amino-acid and carbohydrate metabolism associated with mental deficiency demand not only prompt clinical suspicion and diagnosis but also continued application of basic physiological chemistry, including nutrition in its broadest aspects.

The pediatrician of the '60s, if committed to the holistic** approach to child health, finds his patient-care time reduced by meetings and conferences, often involving members of other disciplines. For instance, the period of time required for "staffing" the post-rubella infant of an unwed mother presents multiple demands, with planning conceivably for the participation of an ophthalmologist, a pediatric cardiologist, and an otolaryngologist, plus a retinue of speech pathologists, occupational and physical therapists, social workers and others necessary to fulfill the total "habilitation" of the child and mother. The direction and speed with which these forces interact insofar as the infant is concerned should be guided by a knowledgable pediatrician. An improvement in the capacity of the physician to deal more productively with these patients and their prob-

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**See Test Your Word Score Page 1491.

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lems is clearly in order. More efficient utilization of ancillary personnel and reorientation of the management of these children in keeping with changing concepts of total care are certainly an important step. Perhaps medical students of today are made more aware of these problems than today's pediatricians were during their education (reference personal).

There exists today a suppositional "super highway" to health. It is intended for unidirectional traffic, although rare iatrogenic reversals are to be seen, e.g., complications associated with vaccination against smallpox. It is this road which we now explore in relation to the pediatrics of tomorrow.

Pediatrics Henceforth

Mortality statistics of the premature and neonate have slowly declined. Increasing fetal salvage, understanding the mechanism initiating labor, and elucidating the pathogenesis of teratology* will so broaden this "highway" that many now "crowded off" early in life will survive. Surgical techniques and instrumentation geared to the exigencies of the immature infant and newborn will further decrease mortality associated with congenital defects — the leading cause of death in the neonate.

Diseases characterized by chronicity will assume greater importance in terms of relative frequency as more attention is directed toward the areas of mental retardation, neurological handicaps, rheumatoid arthritis, and chronic renal disease.

The pediatrician may find that his course is frequently detoured as other disciplines become responsible for areas of patient care. He must remain responsible, however, for the programming of ongoing care, and should avoid the temptation to abdicate, expensive as this may become, as far as expenditure of time is concerned. More and more children will indeed require larger and larger units of attention, and parents will deserve comparable periods for explanation and planning. To some extent the pediatrician will be involved in these sessions.

Rheumatoid arthritis, chronic renal diseases, mental retardation, and neurologically handicapping disorders, must have the same "access rights" to this "highway to health" that have been granted to the polio community — a hamlet now virtually extinct. Current research programs give promise of widening and shortening "access routes" for these somewhat forgotten children.

Rheumatoid arthritis appears to represent an infectious process, and if this is true, appropriate antimicrobial therapy should be possible. Until this is proven, however, physiotherapy, encouragement, and proper medical management must suffice.

The judicious use of corticosteroids to facilitate physiotherapy is occasionally required, but salicylates and hydrotherapy usually control joint involvement. It is imperative to consider the nature of the disease — it is crippling, not killing — and tragic consequences attend the overenthusiastic use of steroids, transfusions, or salicylates. The physician must supply a supportive role and accept along with the patient the chronic, undulating course rheumatoid arthritis pursues.

Chronic renal disease, secondary to acute glomerulonephritis and diabetes mellitus, or of unknown etiology, presents a less hopeful situation. Azotemia, anemia, and ultimate death are now all too common; yet in the practice of tomorrow consideration of the multiple facets of organ transplantation will be necessary. The sacrifice of a kidney from a healthy donor — mother, sibling, or other relative — should be associated with a great deal of counseling of all parties concerned.

The Mentally Handicapped

The problems of children with mental retardation and neurological handicaps will be responsible for a shift of emphasis towards "maximum stimulation" of the individual's potential for development during the pediatric years of life. Unfortunately, an apathetic attitude on the part of some physicians is encountered by parents when their mentally deficient children are examined; an attitude that must improve to encompass hopefully all the advances modern medicine has to offer. There will be an increased need for pediatricians devoted to this particular type

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*See Test Your Word Score Page 1491.

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of patient, as the image of mental retardation emerges from the hidden, secretive aura of the last century into a more enlightened, understanding era, in which shame on the part of parents yields to eagerness to know more about the causes of retardation. Groups of parents to whom the pediatrician can relate freely may be an effective means of public education. Quite likely an increasing proportion of mentally retarded infants will be cared for in the home. The physician, therefore, may expect to see more of these patients who formerly might have been committed to state institutions in the neonatal period.

Pediatrics must meet the challenges inherent in the education of medical students, interns and residents, and in the postgraduate programs for other physicians. Participation in teaching activities is a stimulating and rewarding experience, and pediatricians have no less to offer than the surgeon, internist, or any other physician dedicated to imparting knowledge.

At this hospital we are pledged to continue this vital role of education. Pediatrics tomorrow will represent a reflection of the data, the clinical acumen, the thirst for knowledge, and the motivation to provide succor for children.

Finally, pediatrics tomorrow must continue to reflect the dedication of physicians of these and yesteryears, whose devotion to the growth and development of children has prompted many of these great advances along the "highway of health."

Homer D. Venters, Jr., M.D.*
St. Paul, Minnesota

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Gardner's Syndrome

THE PATIENT of Doctors Shook and Windschitl* who has Gardner's syndrome clearly demonstrates the need for familiarity with syndromes. While our knowledge of many is extremely inchoate, nevertheless, there is a moral responsibility to recognize the signs of at least the most serious ones.

The infrequency with which this syndrome is reported does not reflect its true incidence. Incomplete physical examination, especially by dental, facial, and cranial roentgenography, the attempt at brevity in case reports, and the purposeful deletion from scientific papers of what appear to be incidental findings (epidermoid cysts, fibromas, osteomas, odontomas, etc.) are factors that may be responsible for their failure to be recorded.

Knowledge of the existence of this syndrome adds immense importance to the "incidental findings," for one facet or more almost always precedes the clinical manifestations of intestinal polyposis. The presence of multiple epidermoid inclusion cysts, fibromas, desmoids, or bony growths, especially of the facial skeleton, should lead to a complete search for the intestinal component. Recording of these incidental findings should be just as mandatory as roentgenographic search for additional intestinal polyps if a single rectal polyp is detected. The discovery of multiple polyps, or of any other component, also places responsibility upon the investigator to search other relatives thoroughly for the stigmata. Because a negative report does not mean that polyps or the

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*See this issue, page 1431.

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understanding... precedes development

The development of chlorothiazide and probenecid were events of major importance, but perhaps even more important for the future was the Renal Research Program by which they were developed. When Merck Sharp & Dohme organized this program in 1943, it was expressing in action some of its basic beliefs about research:

- Many problems connected with renal structure and function were still undefined or unsolved. The Renal Research Program would begin its basic research in some of these problem areas.
- From knowledge thus acquired might come clues to the development of new therapeutic agents of significant value to the physician.

For example, the Renal Research Program put fifteen years into this search before chlorothiazide became available. But because these years had first led to a greater understanding of basic problems, the desired criteria for chlorothiazide existed before the drug was developed.

Along with other research teams at Merck Sharp & Dohme, the Renal Research Program continues to add new understanding of basic problems—understanding which will lead to important new therapeutic agents.

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where today's theory is tomorrow's therapy

other components will not appear in future years, periodic re-examination of all persons with a parent who had one or more of the stigmata is necessary. It is also important to inform the patient of the legacy with which he may endow his descendants and the possibility of the existence of the syndrome in his siblings.

Other syndromes may also be cited to emphasize this point. Labial and oral mucosal papillomatosis accompanied by papillomatosis and pigmentation of the axilla, neck and groin signify the development of gastric cancer (malignant acanthosis nigricans). Multiple melanotic spots around and in the mouth, on the eyelids and around the nostrils may signify nonmalignant intestinal polyposis which can cause intussusception and intestinal obstruction (Peutz-Jeghers Syndrome*). Obscure signs as bifid rib, kyphoscoliosis,* falx calcification and multiple cysts of the jaw bones may be associated with multiple basal cell cancers of the skin. Bowen's disease of the skin and dermatomyositis are associated with a higher incidence of internal malignancy.

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Professor in Oral Pathology
University of Minnesota

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*See this issue, page 1468.
**See Test Your Word Score Page 1491.

Mitral Insufficiency with Coronary Disease

THERE ARE many ways in which the cardiac alterations in coronary disease can produce mitral insufficiency. Left ventricular enlargement in cardiac decompensation often is associated with a systolic murmur which later disappears coincident with compensation and reduction in heart size. There are many explanations for this evanescent murmur, including mitral annular enlargement and papillary muscle dislocation. Burchell and Brown[1] describe an unusual (possibly unique) association of mitral insufficiency and coronary disease in a 14-year-old boy submitted to surgery for mitral insufficiency. Anomalous coronary circulation was found five months later at autopsy. The left coronary artery arose from the pulmonary artery.

With myocardial infarction associated complications can cause mitral insufficiency. A left ventricular mural thrombus can interfere with the seating of the valve. Ventricular aneurysm can dislocate papillary muscles and attached valve leaflets. The papillary muscle may be involved in the infarct. Rupture of a papillary muscle is a well recognized complication. The effect of papillary muscle dysfunction without rupture has been recently described in this issue.* Burns and Layman report a case of this type with mitral insufficiency caused by infarcted papillary muscles. The valvular complications of papillary muscle infarction have been emphasized by Burch et al.[2] Burch's group has described an electrocardiographic "syndrome" of infarction of the left anterolateral papillary muscle. They emphasize S-T interval and T wave changes in the left precordial leads with junctional depression of the S-T segment. Electrocardiographic changes in these leads are very common, however, and their suggestion of a "syndrome" which may be diagnostic of papillary muscle involvement remains to be confirmed. In the case described by Burns and Layman electrocardiographic features were not diagnostic.

The subendocardial regions are the distal areas of myocardial circulation and the first to succumb to inadequate circulation. The papillary muscular increscences from the subendocardium are terminal areas whose circulation should be most readily compromised.

Myocardial infarction occurring in the presence of severe mitral (or other valve) disease raises formidable diagnostic problems. Every symptom, sign, or finding of the infarct may be attributed to the valvular disease or to myocardial alteration produced by the orificial problem. The surgeon remov-

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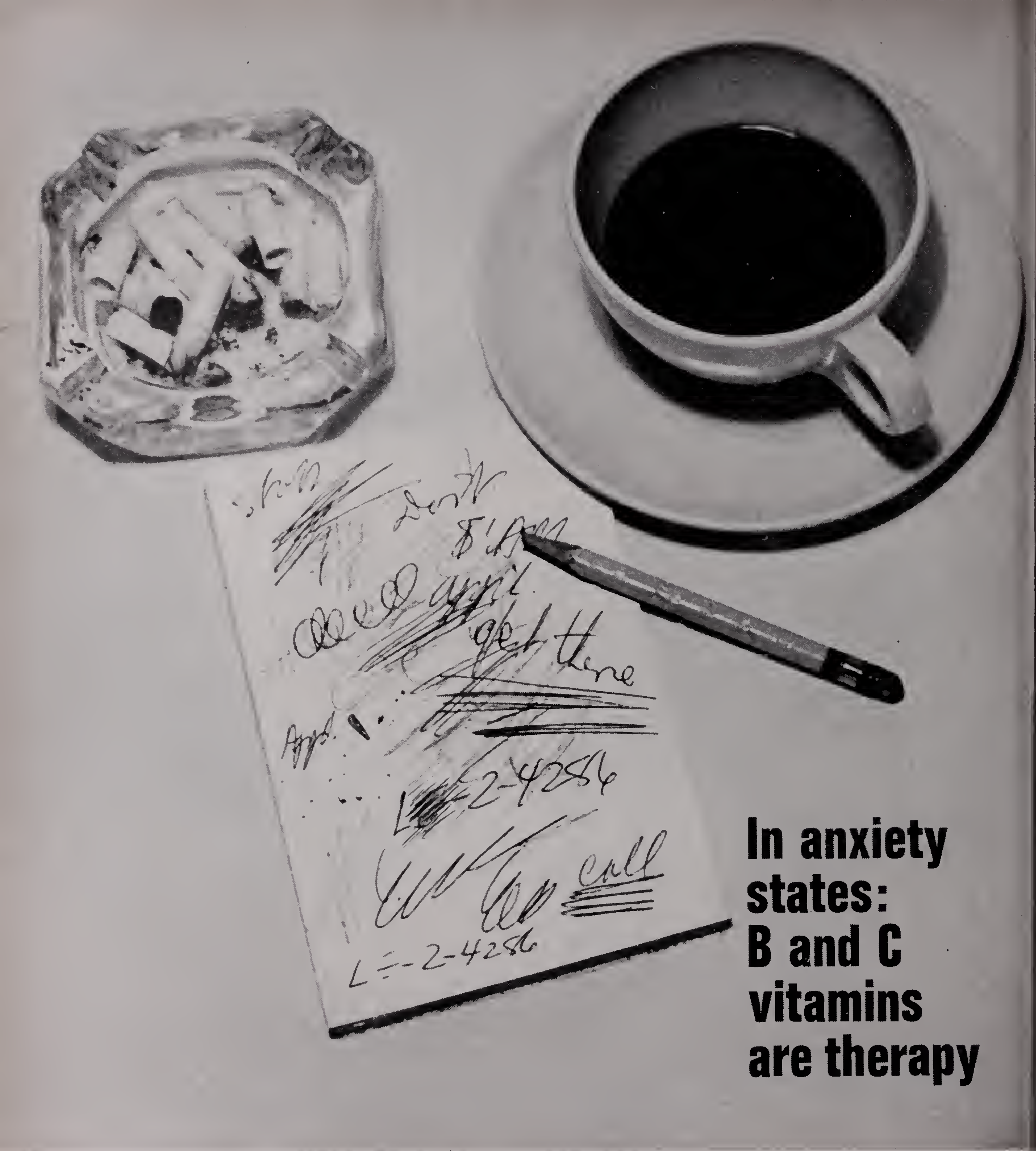
*See this issue, page 1458.



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ing the mitral valve apparatus for replacement with an artificial valve will occasionally be surprised to find an infarcted papillary muscle. This occurred in a 54-year-old man with mitral stenosis and insufficiency.[5]

Surgery of mitral incompetence so far has been concerned largely with rheumatic defects. Corrective procedures may also be possible in a papillary muscular problem. Direct papillary muscle repair has been reported in two cases from the Minneapolis Veterans Administration Hospital by Adicoff et al.[3] Both died in the immediate postoperative period. Prosthetic valves may be considered when intractable heart failure is thought to be due principally to the valve incompetence. However, as Holloway et al.[4] point out, the prognosis must be poor due to the inadequate coronary circulation and the likelihood of further infarction.

Reuben Berman, M.D.
Minneapolis, Minnesota

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Heart Failure in Pediatrics*

IN THE pediatric age group congenital heart disease is the most common cause of heart failure. Infancy is the age when it is most prevalent and when most deaths occur. In past decades rheumatic fever was in the vanguard as a cause of cardiac failure in pediatrics. This disease has become more mild in its manner of occurrence, and its prevention by adequately treating streptococcal disease has made it second in importance to congenital heart disease as a cause of heart failure.

Modern surgery has made possible the salvation of many patients born with congenitally defective hearts. The recognition of the existence of congenital heart disease and the exact definition of the nature of the problem before the patient is in serious trouble are essential to successful outcome. This is particularly true of the infant. In this age group time between first symptoms and death may be very short. Medical treatment should be given but a brief trial and diagnostic procedures carried out concurrently. Severe pulmonary stenosis, aortic stenosis, and coarctation of the aorta are examples of conditions that sometimes require surgical relief soon after symptoms occur if death is to be prevented. Diagnostic procedures can be carried out safely on infants and even newborns. Ignorance of the nature of a problem may be a much greater risk.

When heart failure does occur, it doesn't necessarily mean disaster. Many patients, especially those with left-sided lesions, for example coarctation of the aorta, may be tided over until a time when surgery can be more safely carried out. The recognition of heart failure in infancy and early childhood is sometimes difficult. The classical signs of pulmonary rales, hepatomegaly, and pulmonary edema frequently are absent. Rapid breathing and persistent wheezing often are the only findings. Hyperpnea may be paroxysmal. It may be evident only on exertion. Fatigue during nursing and a longer nursing time may be important historical facts brought forth by the mother. Physical signs that are thought to suggest asthma or bronchitis may be caused by heart failure.

Digitalis in all forms is generally well tolerated in rather large doses by pediatric patients. Notable exceptions are the premature and the newborn infant. Fatalities from

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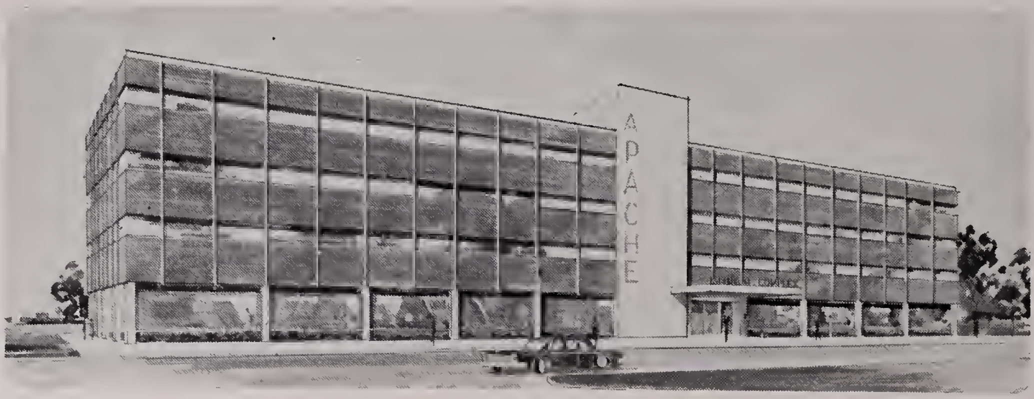

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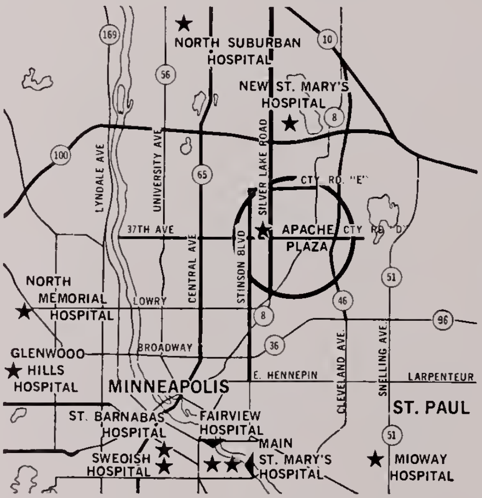
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digitoxicity in these patients are thought to go unrecognized since dysrhythmias are commonly the only manifestation and are recognized primarily by the electrocardiogram. Adherence to the dosage schedule suggested by Doctor Lade in this issue* and frequent evaluation of the electrocardiogram can prevent fatalities. Lanatoside C, Cedilanid, is a more rapid acting glycoside than Lanoxin and there is an advantage in giving the glycoside intravenously to the patient in severe heart failure. Capillary stasis accompanies heart failure and impedes the absorption of digitalis when given intramuscularly or subcutaneously.

Mistakes in calculating the volume of injectible digitalis may be avoided by dilution of the drug and by the use of a tuberculin syringe. Physician attention to these details may help pediatric nurses avoid fatal errors and upgrade the accuracy of administration of other drugs.

George W. Lund, M.D.
Minneapolis, Minnesota

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*See this issue, page 1425.

Test Your Word Score

Catecholamines — *adrenalin-like substances* (page 1425).

Desmoid — *fibrous* (page 1431).

Marsupialization — *an operation opening a tumor, emptying its contents, and stretching its edges to the edges of the external incision* (page 1442).

Spiritus frumenti — *whiskey* (page 1446).

Ethanolic — *having the character of ethyl alcohol* (page 1446).

Thalassemia — *a familial, hypochromic anemia with numerous normoblasts in the blood (Cooley's anemia)* (page 1446).

Hyposthenuria — *secretion of urine of abnormally low specific gravity* (page 1447).

Trepopnea — *where breathing is comfortable in one position and not in another* (page 1450).

Hypercapnia — *excess of carbon monoxide in the blood* (page 1454).

Hippocampal — *pertaining to the submerged ridge forming part of the olfactory cerebral cortex* (page 1454).

Chromatolysis — *solution and disintegration of chromatin* (page 1464).

Holistic — *functioning as a complete, integrated unit* (page 1481).

Teratology — *the division of embryology and pathology dealing with malformations* (page 1483).

Kyphoscoliosis — *backward and lateral curvature of the spine* (page 1487).

Spondylolisthesis — *forward displacement of one vertebral disc over another* (page 1511).

Imprecations — *curses* (page 1513).

Arachnodactyly — *a condition characterized by abnormally long and slender fingers and toes (Marfan's syndrome)* (page 1531).

Extracorporeal circulation — *circulation of the blood outside the body* (page 1545).

Mom says: The fallacy of the written word is that it's there in black and white, so it must be true. — C. O. R.

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Each capsule contains:	
Butazolidin, brand of phenylbutazone	100 mg.
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Geigy

Therapeutic Effects
The acute phase of subdeltoid bursitis, tendinitis and associated periarticular inflammation usually responds promptly and dramatically to phenylbutazone. Pain and tenderness may be relieved within 24-48 hours and mobility of the affected arm quickly restored. Full recovery is frequently achieved within 7-10 days so that therapy is generally of short duration. Calcific deposits are not specifically affected by treatment, but their presence does not appear to retard symptomatic improvement.

Phenylbutazone has not replaced physiotherapy, x-ray treatment, or local injections of hydrocortisone in the more chronic conditions, but it may advantageously be combined with these measures.

Contraindications
Edema, danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. Because of the increased possibility of toxic reactions, the drug should not be given when the patient is senile, or when other potent chemotherapeutic agents are given concurrently. Large doses of Butazolidin alka are contraindicated in patients with glaucoma.

Precautions
Before prescribing, the physician should obtain a detailed history and perform a complete physical and laboratory examination, including a blood count. The patient should be kept under close supervision and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools. Regular blood counts should be made. The drug should be used with greater care in the elderly.

Warning
If coumarin-type anticoagulants are given simultaneously, the physician should watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea and sulfonamide-type agents and insulin. Patients receiving such concomitant therapy should be carefully observed for this effect.

Adverse Reactions
The most common adverse reactions are nausea, edema and drug rash. The drug may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, generalized allergic reaction, stomatitis, salivary gland enlargement, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia are also possible side effects. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently.

Average Dosage
Initially, give 400 mg. daily (one capsule q.i.d), reducing this, if possible, when a favorable therapeutic effect has been obtained. If after one week there has been no response, discontinue the drug. Butazolidin alka contains antacids and an antispasmodic to minimize gastric upset.

Note: The physician should be fully aware of dosage, precautions, adverse reactions, and contraindications as contained in the complete prescribing information.

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Tablets of 100 mg.

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Letter to the Editor:

We are not fooling. We have recently lost two competent physicians in Roseau who have gone away to specialize "for more time off and other benefits." We are really hurting and, I suppose, building up potential coronary disease from lack of sleep and constant jangling of the phone, office and hospital pressure, and from the ever increasing paper work which robs us of the few leisure moments we might otherwise grab.

I think the time is urgent for a crash program to produce more good highly trained general practitioners for the rural and suburban areas. There will always be plenty of specialists and researchers even though the medical schools seem to think otherwise —

Jack Delmore, M.D.
Roseau, Minnesota

Editor's Note: Dr. Delmore's distress call could not be more poignantly stated. Many others have expressed a similar view. At the expense of utter exhaustion no ethical doctor will ever shirk his duty to his patient. He will not prescribe or operate unnecessarily. He will not substantiate unjust claims against the numerous government and insurance guarantors who seem to be ever increasing their demands for superfluous paper work, nor will he perjure himself or the honorable profession of medicine by making charges that are not commensurate with the services rendered. On the other hand, as long as our country remains free from dictators or dynasties, he will not consent to be assigned to a location in Toonerville where he must of necessity be required to revert to the primitive practice of grandfather's day, because he knows that without honorable, ethical, highgrade, modern medicine only the patient suffers.

The Editor's Soliloquy

Cuneiform Symbols

If you have ever tried to read the longhand notes of most physicians on hospital records, you can readily appreciate the difficulty archaeologists encountered deciphering the prescriptions written on stone in cuneiform symbols during the third dynasty of Ur in the year 2100 B.C.

Now realizing these earlier difficulties, some modern hospitals, apparently with the intention of preserving their obsolete records for some archaeologist of the 60th century, have instituted the use of a dictating-typing service whereby doctors' notes can be transcribed into uniformly readable records to repose in and augment future medical archives.

Even though the project would involve the elimination of fascinating, but withal baffling, individualistic graphologies, the common denominator of legibility would be well worth the sacrifice.

Without such a transcription service how would future archaeologists decipher the numerous chirographies encountered in present medical records: the strabismic micrography of U. S. H., the gargantuan macrography of V. L. H., the execrable cacography of H. B., and the exasperating haplography of H. W. O. Of course those 60th century archivists et al. would have no trouble whatsoever perusing the delightful calligraphy appearing above the initials C. O. R.

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Indications: 'Miltown' (meprobamate) is effective in relief of anxiety and tension states. Also as adjunctive therapy when anxiety may be a causative or otherwise disturbing factor. Although not a hypnotic, 'Miltown' fosters normal sleep through both its anti-anxiety and muscle-relaxant properties.

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Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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Curbstone Consultation

Drug Sensitivity Hepatitis

QUESTION: Is the drug sensitivity hepatitis amenable to any specific type of therapy?

ANSWER: The first principle of therapy is recognition of the drug-induced nature of the hepatic injury followed by withdrawal of the drug. For cholestatic reactions such as those produced by sulfonylurea compounds such as chlorpromazine or anabolic steroids, further therapy is usually not needed. If pruritus is severe, cholestyramine will be of some help when it becomes available. Periactin 4 mg. q.i.d. may also be helpful. In general, patience, on the part of the patient and also the doctor, is what is needed most. The role of bed rest has yet to be evaluated in this condition, but some restriction of activity seems reasonable. The viral hepatitis-like reaction seen with monoamine oxidase inhibitors and now being reported with halothane is treated like any severe viral hepatitis with cortico-steroid therapy if the patient becomes very ill.

Fenton Schaffner, M.D.
Mt. Sinai Hospital
New York, New York

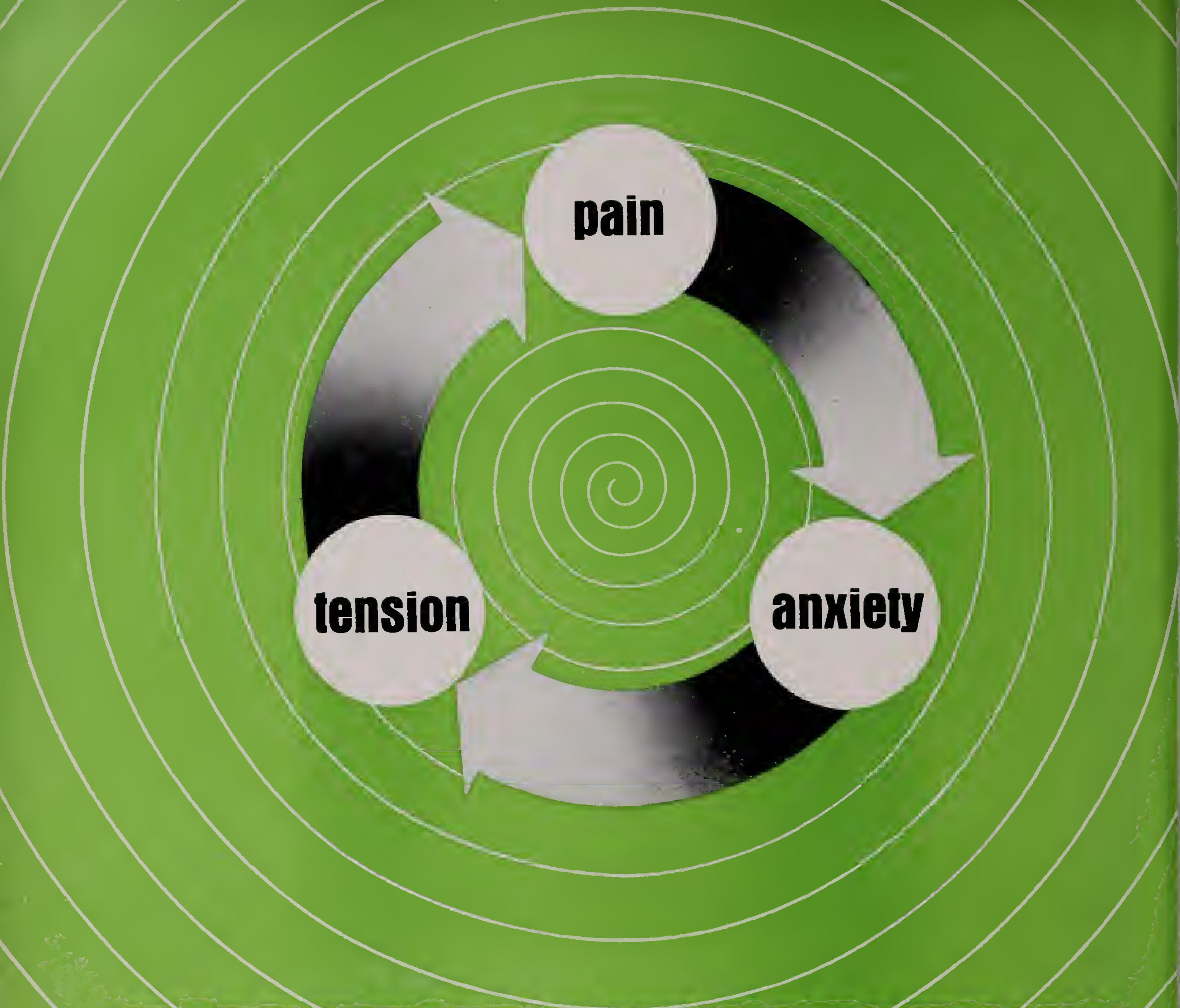
Progestin-Estrogen

QUESTION: Do you have any method of selecting suitable cases of acne which will respond favorably to the progestin-estrogen drug therapy?

ANSWER: I do not believe this type of therapy should be used as routine. Many female patients with acne will respond to the more conventionally used types of therapy and do not necessitate the use of hormones. We reserve hormone therapy for those patients who have not responded to a more conservative approach, including the use of acne surgery, topical medications and antibiotics. Naturally, the patients that are selected are among those who are in their upper teens or early twenties.

John S. Strauss, M.D.
Associate Professor
Boston University
Boston, Mass.

"The value of a gift lies not so much in the price tag as in the love tag." — Dr. E. O.



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In tension headache

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Side effects such as gastric distress, occasional weakness, sedation or dizziness may be noted. Ordinarily, these may be reversed by a reduction in dosage or temporary withdrawal of the drug. TRANCO-GESIC should not be administered to persons known or suspected to have an idiosyncrasy to acetylsalicylic acid.

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Fracture–Trauma Conference

Management of the Acutely Injured Patient

The highest mortality among acutely injured patients occurs within the first few hours following injury. Therefore the initial evaluation and treatment of these patients is critical if deaths are to be prevented.

Although many patients with massive injuries involving aortic and/or myocardial disruption, head injuries, or liver rupture die prior to their reaching medical help, yet other pateints with similarly massive injuries may still be alive and therefore potentially salvageable at the time of their arrival at a medical facility. Pertinent evaluation and treatment must be rapidly initiated to help this type of patient. A report from the rescue personnel should be filed, including mode of injury, initial and subsequent changes in level of consciousness, treatment given, and estimated prior blood loss including that at the accident scene.

Dangers of Mobilization

Active or passive motion of the acutely injured patient is to be avoided for several reasons.

Loss of Blood Volume

A patient may lose up to 20% of his blood volume and through compensatory vasoconstriction and selective circulation maintain a relatively normal measurable arterial pressure. The seemingly minor further trauma of transfer to an x-ray table may initiate profound shock in such a patient.

Hypotension

Further bleeding at fracture sites or from ruptured viscera occasioned by even slight motion of the patient may similarly produce severe hypotension with resultant myocardial and cerebral damage. Pelvic fractures, occult and unsuspected prior to x-ray examination, are particularly treacherous in this regard. Hauser[1] has shown the massive and often lethal occult bleeding that can occur in these circumstances. Even passive motion of these patients may initiate further massive unobserved blood losses.

Continued

Transection of Cord

Unsuspected spine fracture-dislocations may on motion be converted from an asymptomatic spinal cord contusion to a complete and permanent cord transection. Therefore we routinely place each acutely injured patient at admission on a radiolucent rigid litter (Fig. 1) developed at the Ancker Hospital.[2] Extremity fractures are stabilized by constant traction, and the head is stabilized by laterally placed sand-bag supports. The patient is maintained continuously on this litter throughout his initial evaluation, x-ray studies and early treatment, be it supportive observation or emergency surgical procedure.

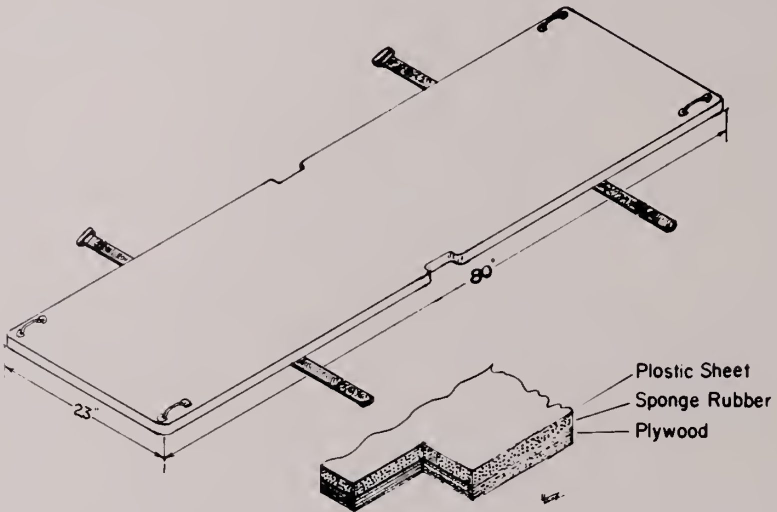

Fig. 1 — Diagram of Receiving Room litter employed at Ancker Hospital.

Correct Respiratory Insufficiency

Initial evaluation of the acutely injured patient must include observation for respiratory distress, cardiac arrest, shock and brain injury. Assignment of priority of treatment usually goes first to respiratory insufficiency, be it of neurological, intrabronchial or extrabronchial origin, because such insufficiency is least well tolerated and must be corrected before any of the following problems can be treated. In close succession follow cardiac arrest, hemorrhagic shock and head injuries, with extremity fractures usually of least initial risk.

Open Airway

The patient's upper and lower respiratory tract is cleared by suction, an oral airway inserted and ventilatory support given by the best method at hand, such as a face mask and a device for administering positive pressure intermittently. This measure failing, insertion of an endotracheal tube may prove necessary; but such a maneuver may cause dangerous delay in pursuit of more urgent matters and should not be done routinely.

Prevent Pneumothorax

Sucking chest wounds should be completely occluded with a vaseline gauze dressing and a chest tube inserted for suction until the patient's vital signs are stable and his total injuries known, when definitive debridement and closure are propitious. Physical signs of a pneumo-and/or hydrothorax are indication for confirmatory thoracentesis, whereupon a large chest catheter should be placed and connected to suction. This maneuver, of very low immediate or long-term risk, prevents the formation of an occult massive pneumothorax or hemothorax when attention may be diverted to another problem. Moreover it allows monitoring of blood losses within the chest. The presence of an unstable area of chest wall with paradoxical respiratory motion — a "flail" chest — is an indication for prompt insertion of a chest tube for suction, performance of a tracheostomy, and positive pressure respiratory assistance. Pulmonary edema will reward delay in this.

Emergent Treatment

Simultaneously the patient's pulse is monitored digitally to detect an unusual or absent cardiac rate. Closed chest massage must be promptly performed for cardiac arrest, all the while its inciting cause being sought and corrected. The rigid litter is ideal for this technique. Arterial blood pressure should be monitored by an arm cuff.

Intravenous

An intravenous drip through a large-bore needle must be placed in an arm or leg vein or both as early as possible, enabling recovery of a blood specimen for typing and cross-matching, and providing constant access to the vascular system not only for the emergency administration of fluid and blood but also of medication, especially as needed to treat cardiac arrest. Moreover, the peripheral venous pressure can thus also be estimated for guidance in blood replacement. To wait until the intravenous is "needed" is to wait too long.

Transfusion

If the patient is hypotensive and the above needs are fulfilled and of course if blood loss is evident, decreased circulating blood volume may be assumed. Brain injuries as a rule do not cause hypotension. Rapid transfusion of Type O Rh negative whole blood or, as secondary choice, dextran or plasma should be given until cross-matched blood is available or normotension ensues. Such transfusion may be diagnostic as well as therapeutic if a rise in arterial pressure occurs. Recurrence of hypotension would indicate continuing losses of blood. Chest blood losses via the chest tubes will be evident, as will enlarging hematomas about peripheral fractures. Rapid blood loss via chest tubes with persistent hypotension despite multiple transfusions is an urgent indication for immediate thoracotomy. However, in the absence of such obvious blood losses the possibility of occult intra-abdominal hemorrhage from an injured viscus or retroperitoneal blood loss from a fractured pelvis or ruptured bladder must be considered.

Bladder Catheter

A Foley catheter should be passed into the bladder for detection of urinary tract bleeding. A cystogram, performed by simply injecting 100 cc. of 50% Hypaque through the catheter and taking one x-ray of the pelvis — portable x-ray equipment is adequate — and another after the

Continued

bladder is emptied, will show extravasation of dye if the bladder is ruptured. The cystogram should be done as soon as the patient's vital signs are stable or before he undergoes emergency laparotomy. An intact bladder in the presence of gross hematuria is an indication for an emergency intravenous pyelogram.

Laparotomy

If hypotension unaccountably and rapidly recurs despite quick administration of 1500 cc. whole blood, intra-abdominal or retroperitoneal hemorrhage is obviously suspect. Persistent shock, increasing abdominal distension and tenderness predicates immediate laparotomy. Under less urgent diagnostic uncertainties possible intra-abdominal hemorrhage or visceral disruption may be accurately detected by a simple technique of diagnostic peritoneal lavage previously described at Ancker Hospital.[3] A #18-F catheter* with many side holes is introduced into the abdomen via a trocar or stab wound. If no blood or enteric content is obtained by simple aspiration, 1000 cc. of a sterile isotonic saline solution is instilled into the abdominal cavity and then aspirated for examination. It is an extremely sensitive test with no false negative or false positive results reported as yet. Perry[4] found the mortality of blunt abdominal trauma, the only type in which decisions against laparotomy must be made, to be 46%, a large part of which was due to undiagnosed visceral damage and hemorrhage. Since the introduction of this technique at Ancker Hospital there have been no cases of undiagnosed intra-abdominal hemorrhage due to blunt trauma.

Comments and Conclusions

Not until the patient's vital signs are stable should he be transported for complete x-ray evaluation. He is maintained with fractures splinted on the radiolucent litter throughout all x-ray examinations. An acutely injured patient should be accompanied to and attended in the x-ray rooms by a nurse or physician for repeated monitoring of his vital signs. The clinical status of such a patient can change quickly.

While attention has been drawn to the dangers and signs of thoracic and abdominal catastrophes secondary to trauma, so must careful attention be directed to the signs of serious brain injuries such as deepening drowsiness, lateralizing pupil dilatation, and peripheral neurologic deficits. Drainage of subdural or epidural hematomas may be life-saving if not delayed. Unrelenting generalized extensor rigidity, coma, and dilated fixed pupils are usually signs of lethal brain-stem damage.

Harlon D. Root, M.D., Ph.D.**
St. Paul, Minnesota

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*Inpersol Catheter by Abbott Laboratories.

**Department of Surgery, Ancker Hospital, St. Paul, Minnesota and University of Minnesota Medical School, Minneapolis, Minnesota.

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Drive Safely

Thou hast a head and so has a pin. — Jonathan Swift

Tumor Conference

Varix of the Duodenum Simulating Duodenal Tumor*

Pathways of collateral blood flow in portal venous congestion develop primarily at the gastroesophageal junction, the hemorrhoidal veins, and the umbilicus. The purpose of this report is to present a patient with Laennec's cirrhosis* in whom a radiographic duodenal mass was found to be a cluster of dilated veins. A review of the literature has failed to reveal any previous description of such a lesion.

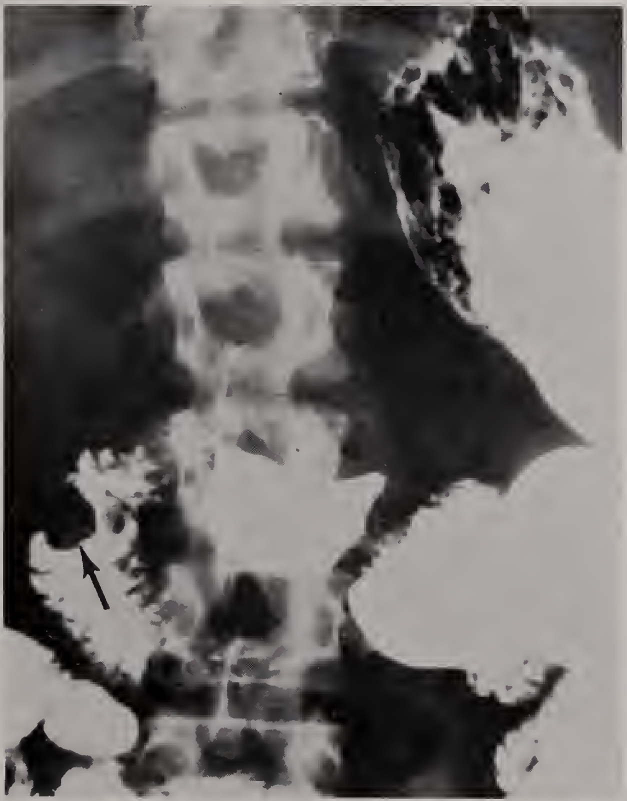

Fig. 1 — Upper gastrointestinal series demonstrating a filling defect (arrow) in the second part of the duodenum in a patient with portal venous congestion. This lesion proved to be a large venous varix.

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*See Laennec's cirrhosis Page 1503.

Continued

Case Report

A 55-year-old female with a history of alcoholism was admitted to the hospital for the seventh time on March 24, 1965, complaining of progressive weakness and shortness of breath. She was known to have Laennec's cirrhosis and had had upper gastrointestinal bleeding and coma previously. Because of a diffuse patchy infiltrate on the chest radiograph and pulmonary function studies demonstrating an alveolar-capillary block, the patient had a diagnostic lung biopsy. The specimen obtained showed sarcoidosis.

While convalescing from this procedure, the patient was noted to have melena, began to have hematemesis, and subsequently required repeated transfusions. An upper gastrointestinal series showed no evidence of esophageal varices but a filling defect, interpreted as a polypoid tumor, was seen in the second part of the duodenum (Figure 1). A previous gastrointestinal series from 1963 did not show this lesion.

Two weeks after the spontaneous cessation of gastrointestinal bleeding an exploratory laparotomy was performed. The mesenteric veins were dilated and tortuous but esophageal varices were not prominent. The duodenum was mobilized and a group of large dilated veins could be seen on the posterior wall of the second part of the duodenum (Figure 2). The varix simulated a mass in the duodenal wall upon palpation and when visualized intraluminally appeared as a group of veins, 2 x 3 cm. in diameter, covered by duodenal mucosa. There was no active bleeding.

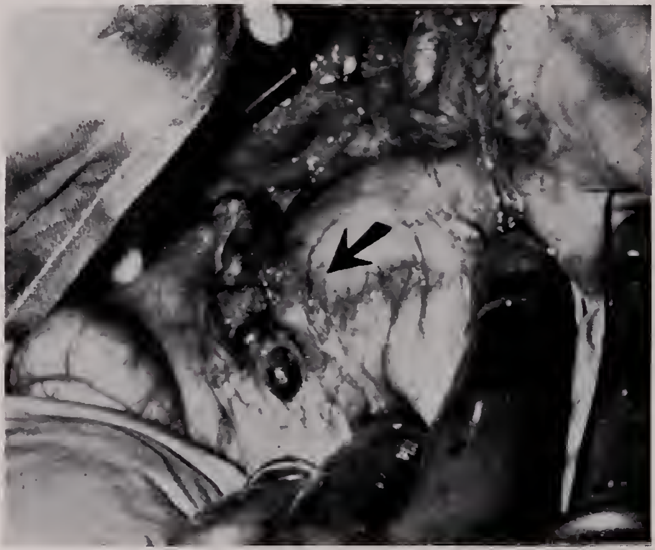

Fig. 2 — Photograph taken at the time of laparotomy in this patient. The duodenum has been mobilized and its descending portion lies just above the surgeon's fingers. The extrinsic part of the varix crosses its posterior aspect (arrow).

Simultaneous measurement of portal and systemic venous pressures revealed a low gradient (portal system = 21 cm. saline, superior vena cava = 10 cm. saline) and a shunting procedure was deemed unnecessary. The varix on the duodenum was thought to constitute a sizable portion of the patient's porto-systemic shunt and was left intact. A vagotomy and gastrojejunostomy were performed to keep the gastric secretions and contents from contacting the lesion. A liver biopsy confirmed the diagnosis of Laennec's cirrhosis.

Discussion

We have been unable to find previous reports of a lesion such as the one described in this patient. Olson et al.,[1] reviewing the radiographic studies in a group of 72 patients with portal venous congestion previously reported by Hallenbeck,[2] found evidence of duodenal deformity in ten. These authors comment on the known association of peptic ulcer disease with hepatic cirrhosis. In their series, however, duodenal deformity was due not to old peptic ulcer disease but rather to compression of the duodenum by dilated venous collaterals. This deformity they describe as occurring about one cm. distal to the pylorus and due to pressure from a dilated posterior superior pancreaticoduodenal vein. The varix found in this case, however, lay in the second portion of the duodenum and does not represent the abnormality described by Olsen although the etiology is probably similar.

Summary

A patient with Laennec's cirrhosis with a duodenal mass is presented. The lesion proved to be a varix caused by portal venous congestion.

Claude V. DeShazo, M.D.*
Robert P. Belin, M.D.*
Judson F. Lloyd, M.D.*
Arnold I. Walder, M.D.**
Minneapolis, Minnesota

From the Department of Surgery, University of Minnesota School of Medicine.
*Medical Fellow, Department of Surgery.
**USPHS Postdoctoral Research Fellow.

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Laennec's Cirrhosis*

A multitude of names (Portal cirrhosis, diffuse nodular cirrhosis, atrophic cirrhosis, hobnail liver, alcoholic cirrhosis) have been used to indicate this disease which is a very common type of cirrhosis observed in all parts of the world.

It is most commonly observed following the long continued use of alcohol, although in some countries it is associated with malnutrition, particularly of protein containing the essential amino acids. A deficiency of lipotrophic substances, especially choline, has been shown to produce fatty livers that progressed to cirrhosis in experimental animals. The administration of alcohol to animals has resulted in the production of cirrhosis when combined with high fat diet in prolonged experiments. The changes which are produced in the liver with marked fatty degeneration are common findings in alcoholism. In this stage it is thought that the process is probably reversible if an adequate diet is provided and if the patient abstains from alcohol.

When the fibrosis increases pseudolobules develops and the process becomes irreversible.

Pathology
W. A. D. Anderson
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*See Page 1501.

Some people pay a compliment as if they expected a receipt. — Frank Hubbard

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Athletic Injuries

The Immediate Management of Abdominal Injuries in Athletics

It is fortunate that abdominal injuries are of infrequent occurrence in athletics, for they are fraught with life-threatening hazard. Football is the only major sport in which there is any significant possibility of abdominal trauma, and even here hip and rib pads protect all but a small portion of the abdomen. Penetrating injuries are so rare, and their management so standardized, that they need no further discussion. The blunt injuries, however, require astute management.

Abdominal injuries of the closed or nonpenetrating type are always difficult to evaluate. Relatively insignificant trauma, affecting only the abdominal wall proper, can cause spasm, guarding, and muscular rigidity which make it almost impossible to rule out deeper and more serious injury to the viscera. As a consequence, in the management of abdominal injuries sustained in athletic activities, one must always err on the conservative side.

An athlete who sustains a blow to the abdomen from which he has not fully recovered after a very few minutes of rest should be taken out of the game and to the locker room. Unlike injuries of the extremities, it is almost impossible to evaluate an abdominal injury on the playing field. Inspection and palpation cannot be adequately performed on the exposed field or court. The injured player should either walk, or be carried to surroundings more conducive to thorough examination.

Inspection of the abdomen, once the injured player has disrobed, may reveal ecchymosis or swelling of some portion of the abdominal wall. Contusions and hematomas of the subcutaneous and muscular layers of the abdominal wall are relatively common, but insignificant. However, when they occur they are frequently associated with tenderness and rigidity, which make it impossible to rule out an underlying injury of a serious nature. In such cases the athlete must refrain from further activity and be kept under careful surveillance until either he gets better or the need for definitive surgery becomes apparent. This may be a matter of hours or even days.

If there is no visual evidence of injury, then a careful palpation of the abdomen should be carried out. The solid organs (liver, spleen and kidney) are most apt to be injured by blunt trauma, but injury to a hollow viscus can occur. The signs associated with the injury depend on the organ involved.

Rupture of a hollow viscus will cause the generalized rigidity associated with peritonitis, and the need for immediate surgery should be obvious. Injuries to solid organs, on the other hand, may not always be associated with prominent symptoms.

Liver injuries, unless they are extensive and include the capsule, may cause only an ill defined tenderness and spasm in the upper abdomen. For this reason even minimal guarding in the liver area requires conservative management and close observation. Increasing hemorrhage or bile leakage from the liver over the next few hours will produce signs and symptoms which warrant laparotomy.

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*See Minnesota Med 48:1359 for second in this series. Sponsored by Minnesota Committee on Trauma of the American College of Surgeons.

Continued

The findings associated with a torn spleen may be the catastrophic ones of acute hemorrhage. Contusions or small lacerations may produce only minimal findings of tenderness and rigidity in the left upper quadrant. Since delayed rupture of the spleen is common, even minimal left upper quadrant tenderness demands continued rest and observation of the patient.

Kidney injury should be suspected if flank tenderness or discoloration is present. Urinalysis will usually help substantiate the diagnosis.

Injuries to other retroperitoneal organs, or retroperitoneal hemorrhage, though they may not be initially associated with significant abdominal tenderness, will frequently cause vomiting and/or absence of bowel sounds. Even in the face of a relatively innocuous abdominal examination these signs are so suggestive of serious injury that a conservative regimen must be followed.

Injuries to the abdominal viscera threaten not only the well being but the life of the injured athlete. Any abdominal trauma that causes more than momentary symptoms must be considered a life threatening injury, and demands conservative management. The "let's take a chance" philosophy, that might be permissible with less potentially lethal injuries, has no place in the management of abdominal trauma.

William A. Nolen, M.D.
Litchfield, Minnesota

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Neurological Conference

Herniated Intervertebral Disc*

Dr. Robert Soll:** The patient today is a 32-year-old housewife who first experienced difficulty with her back approximately one year ago. She and her husband had been in the process of remodeling their home, and this activity included carrying sheet rock. As a result the patient had been doing a fair amount of lifting. One day while reaching for an object on a high shelf with her right hand, she felt a sudden sharp "pulling" sensation which radiated down her right leg into her toes. This discomfort persisted without change and was present almost constantly. During the ensuing months the pain gradually became more severe, finally requiring hospitalization of the patient. She was placed in pelvic traction in the hospital for approximately two weeks; the traction being increased to 20 pounds without relieving the patient's discomfort. She was subsequently referred to the University Hospitals for further evaluation.

For the past seven or eight years the patient has had minor back trouble described as a mild backache primarily in the lumbar area of the spine. She has also had some aching in her neck which has been associated with a headache at times. On one occasion she was told that her right leg was one half inch shorter than her left; therefore, she was treated with a shoe lift which she has worn ever since. The patient herself has not been certain of any benefit received from this shoe lift.

The general physical examination was within normal limits except for a mild scoliosis of the lumbar spine, which had a convexity to the left, and was associated with a slight pelvic tilt. On neurological examination the cranial nerves were found intact. The deep tendon reflexes were equal bilaterally in the upper extremities and at the knees, but the right ankle jerk was absent. There was weakness of both dorsiflexion and plantar flexion of the right foot, and an area of hypesthesia was present over the lateral aspect of the right lower leg and dorsum of the right foot. Straight leg raising elicited pain in the posterior right thigh and buttocks; deep palpation of the posterior thigh and buttocks produced tenderness along the course of the right sciatic nerve.

Continued

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*Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatric conferences are held the first and third Wednesdays of every month from 3:15 to 4:15 p.m. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Charles Branthaver, in Pediatrics, and Dr. Robert Soll, in Adult Neurology. This conference was held Thursday, February 18, 1965, at 4 p.m.

**Adult Neurology and Moderator, University of Minnesota Hospitals.

Dr. John Brantner:* One can easily guess from talking with the patient what the results would be on her Minnesota Multiphasic Test. She is a cheerful, happy person. The test is completely normal in every respect. There was no depression or anxiety and her hysteria is high. She has some physical complaints but not many, and she is optimistic about the future. As far as the low back pain scale is concerned, I have no idea what it means in patients after surgery. Because of this large hysterical component her scale was in the border-line range of normal. However, it is difficult to apply this result to a patient who has already had surgery.

Dr. Richard Magraw:** Could you explain to us what the low back pain scale is?

Dr. Brantner: This scale was developed in an experimental attempt on the Minnesota Multiphasic to differentiate between patients whose low back pain was due to disc pathology proven by surgery and those who had low back pain with no demonstrable pathological changes at the time of surgery. It is rarely interpreted by itself; but, added to other information, it supplies one additional piece of evidence for or against the hypothesis of an organic cause of low back pain. Sometimes one finds an "organic" low back pain scale along with a Multiphasic, suggesting hypochondriasis or a conversion reaction. This helps in those cases in which a basically hysterical or hypochondriacal person develops low back pain due to an organic cause.

Dr. Lyle French:† This lady had signs and symptoms of an intervertebral disc compressing *the fifth lumbar nerve* which is usually compressed by a disc located between the fourth lumbar and the fifth lumbar vertebrae. This was chiefly manifested by numbness and weakness of her right great toe with a diminished right Achilles reflex. If *the first sacral nerve* had been involved, the numbness would have been along the lateral aspect of the foot and calf and she wouldn't have had any weakness of her great toe. The small lesion that is demonstrated on the myelogram is located between the fourth lumbar and fifth lumbar vertebrae and thus fits with the physical findings. One has to be careful in localizing these lesions in order to determine accurately the proper site of operation; one should appreciate the fact that it is easy to be thrown off one cord level. This defect corresponds to the one that we found at the time of surgery.

Dr. Soll: I would like to emphasize also that the history can be of great importance in characterizing the type of herniation that exists. Commonly, back pain associated with disc disease is accentuated in the erect position and tends to be relieved by lying down. It must be kept in mind, however, that the reverse situation can paradoxically exist, that is, pain can be increased by lying down and can be relieved by getting up and walking. The explanation that is usually given for this phenomenon is that an extruded disc has compressed and fixed a nerve at one of the intervertebral foraminae. Upon lying down the weight of the body is removed from the spinal column and there is a tendency for a gradual lengthening of the column to occur as a result of an expansion of the intervertebral discs. Normally the spinal nerves can compensate for this stretching by freely moving within the intervertebral foraminae; however, if a spinal nerve has been fixed by an extruded disc, the nerve itself becomes stretched, thus eliciting pain which can be relieved by again arising and walking around until the spinal column gradually shortens. This paradoxical history should be remembered in those cases in which a disc is suspected. Dr. French, would you describe the operation which you performed on this patient?

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*Assistant professor clinical psychology, University of Minnesota Hospitals.

**Director, Comprehensive Clinic Program, University of Minnesota Hospitals.

†Professor and director neurosurgery, University of Minnesota Hospitals.

Dr. French: We performed the usual operation for a herniated disc. In this situation the patient is lying prone. A six-inch vertical incision is made in the mid-line centered over the spinous processes overlying the region of the involved disc. The erector spinae muscles are separated from the spinous processes and from the laminae, thus exposing the ligamentum flavum. A hemilaminectomy is then performed in which a little bit of bone is removed from the laminae above and below the lesion. This actually leaves the laminae still intact and strong. We do not go out to the articular facet, as this would weaken the spine. Thus the dural sac is exposed and the nerve root comes into view laterally where it is being compressed by the protruding disc. The posterior longitudinal ligament is incised, and we then go down into the interspace and remove the cartilaginous disc tissue from within the center of the intervertebral disc as well as that part which has herniated. All the disc is not removed but rather approximately two thirds of the total disc tissue. This particular patient had a degenerative disc, but not a completely extruded, free-fragment type disc such as those encountered at times after a severe injury. Completely extruded discs often occur after falls from very high places, such as from a ladder. With these types of accidents a piece of disc may herniate which often can be as large as the tip of one's thumb. This patient did not have this type of disc; her disc was one which results from chronic degenerative changes. Acute symptoms are usually precipitated by a lesser injury which permits sudden disruption of the disc. Subsequently, the gradual wear and tear of ordinary life will make the disc degenerate more and more; thus it will progressively bulge out farther, increasing the symptoms with the passage of time. Twisting and turning movements are particularly apt to aggravate this type of disc degeneration and we advise patients to minimize such activity. An example of such activity is bowling, which requires bending and twisting movements of the back which should be avoided. After the disc is removed we simply suture the fascial layers together, closing the wound.

Dr. Magraw: Does the disc ever become very soft?

Dr. French: I don't believe there is ever any real liquefaction of the disc, although this term is used. The intervertebral disc will not dissolve; thus disability caused by it will not disappear; likewise it will not be resorbed or diminished. The lesion is fundamentally due to a break in the continuity of the posterior longitudinal ligament. Rotation of the spine produces a twist in the annulus fibrosus which is the outer part of the intervertebral disc enclosing the nucleus pulposus. As a result of this twist the nutrition to the nucleus pulposus, which is actually a remnant of the original notochord, is reduced. The nucleus pulposus then gradually degenerates and extrudes through a crack in the annulus fibrosus. Occasionally a degenerative disc may gradually extrude part way producing symptoms; manipulations of the back can sometimes work this disc back into its proper location, thus relieving the symptoms.

Dr. Magraw: Are there any microscopic changes in the disc itself?

Continued

Dr. French: Yes, there are microscopic changes. There are also chemical changes. The character of the nuclei in the nucleus pulposus itself is changed and the character of the chondroitin sulfuric acid is changed. The main point is that once one has an early disc, any further wear and tear of everyday life is going to make it worse. If one adds the aggravation of a quick twisting movement, a sudden fall, or overweight, the condition will become much worse.

Student doctor: What happens to the intervertebral space once the disc has been removed?

Dr. French: The vertebrae simply settle together. Actually they probably have already settled together somewhat because the disc tissue has partially extruded. Fibrosis gradually occurs in the area from which the disc tissue has been removed and, in some respects, the area probably becomes even stronger eventually than it was prior to the illness.

Student doctor: What are Williams' exercises?

Dr. French: Williams' exercises are a series of exercises to strengthen the back muscles. Frankly, I feel that Williams' exercises are to some extent good but also in other respects bad for degenerative disc disease. Those exercises that include raising and lowering the legs when one is lying down to help increase the tone of the back and abdominal muscles are good. In the shower, movements such as stretching and raising the arms above the head also allow gentle exercise of the muscles and help to increase their strength and tone. Other exercises, however, such as violent twists or turns and touching the toes, produce a lot of extra stress on the back, only aggravating degenerative changes.

Student doctor: Will traction improve a herniated lumbar disc?

Dr. French: Usually pelvic traction for a herniated lumbar disc does no good other than to keep a patient in bed. If there are symptoms of a cervical herniated disc, traction may tend to relieve the patient; but I feel that the idea of trying to pull out the strongest muscles on an individual's body like the back musculature by traction on the legs or hips is not feasible. It would be better simply to keep a patient in bed in a somewhat flexed position; such a position puts less stress and strain on the muscles of the back, thus reducing the muscle spasm and occasionally relieving the pain. At times manipulations of the back similar to chiropractic manipulations may cause symptoms abruptly to disappear.

Dr. Magraw: What proportion of patients pick up their bed and walk after disc surgery

Dr. French: I think this varies greatly, depending on the character of the disc and also on the type of person who is having the operation. In an industrial case in which a man would earn $42.50 if he didn't work, and $44.50 if he did, it would be difficult to get him right back on the job; this would be especially true if he were 54 years of age, had been doing hard labor all of his life and was getting tired of it. If one selects only individuals who have a good clear-cut disc syndrome, who are energetic and depending on steady employment to make a living, they will not only go back to work before two months, which is the usual time for an industrial case to return, but they will usually recover within two to four weeks time. I don't believe I have ever operated on truly private entrepreneurs with no income unless they worked, who didn't return to work within two or three weeks. There are also many other people who fit into this category. A classic example in my own experience was a navy pilot who had three years to go before his retirement. At that time he couldn't walk or sit because of symptoms of a herniated lumbar disc. If he had been retired because of disability, his retirement pay from the navy would have been very low. He entered the hospital on a Friday night; I operated on him the next morning; and he returned to work the following Monday morning. No one in his outfit even knew that he was ill. I think that if we took all farmers and operated on them, 90% of them would go back to work soon. If we took all industrial cases, including work such as carrying a quarter of beef, driving a truck across the country or lifting sacks of potatoes, 50% would soon return to work. If we considered a group of people in the 50 to 55 year age group who have been working for someone, they would remain out of work for two, three or four months and then gradually return to their jobs. Altogether 70 to 75% of these patients will eventually return to full time work. There is this variation.

Student doctor: What activities do you instruct patients to avoid?

Dr. French: I tell them to avoid lifting very heavy weights and any violent twisting movements; I also tell them specifically to quit bowling. Bowling is a very poor sport for people with back trouble. I also feel that a patient should not drive a car long distances without stopping periodically every hundred miles or so to get out and stretch. This type of strain wouldn't actually cause a recurrence of a disc but it does stiffen back muscles, thus causing low back pain due to muscle spasm.

Dr. Soll: Is there a specific indication for an anterior approach to a herniated disc?

Dr. French: Yes, I don't believe anybody does an anterior approach to the ordinary herniated intervertebral disc. Anterior approaches are done when a secondary fusion of the vertebrae is planned. Such a fusion would be indicated in people who have had a number of operations for discs and not been relieved of pain. The hope is that this type of fusion will alleviate some of the symptomatology. Posterior fusions have been shown not to be of much benefit as far as fixation of the spine is concerned. There are several reasons for poor results after removal of an intervertebral disc: first, a patient may not have a herniated disc at all but rather some other lesion, such as a spinal cord tumor, spondylolisthesis,* or an anxiety state in which the complaint is "oh, my aching back;" second, the surgeon may not do an entirely neat job as far as the excision of the disc tissue is concerned; for example, the nerve roots may be traumatized, the dura may be torn, there may be too much bleeding in the operative area, or all the disc tissue may not be found. At times this tissue may extrude far laterally and may not be discovered unless looked for specifically. I am discussing all the things that could happen; I don't mean to imply that all these things necessarily do happen. Finally, a patient may have just reached that time in his life when he has lost the desire to continue working. This last possibility may be the result of aging, dislike for the boss, or a feeling that his wife should start working instead of just lying around. There are a lot of reasons for which one could get poor results.

THE PATIENT ENTERS THE ROOM FOR QUESTIONING

Dr. Soll: (to the patient) Would you tell us what your pain was like initially?

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*See Test Your Word Score Page 1491.

Continued

Patient: When I first got the pain, it was like a line going up my leg to my hip. It was quite sharp. The pain later just grew from there and became a throbbing in my ankle, knee, and hip. I didn't have any real backache to speak of until just lately. Recently I have noticed a stiffness in my spine. Of course, I did have a lot of pain when I was in traction last fall.

Dr. Soll: Was it worse in traction than when traction was not applied?

Patient: Not especially, but I did feel tingling in my toes when I was in traction. First it was in my little toes but later the big toe was affected also. Just having a sheet over my foot was painful.

Dr. Soll: Was the pain any worse when lying down in contrast to being up and about?

Patient: If I could be up for about an hour and then stay up it would be better, otherwise it would be better when I was lying down.

Dr. Soll: Did you ever have to get up at night to walk it off?

Patient: No, that would do no good unless I could be up at least an hour.

Dr. Soll: Has the pain changed any since the operation?

Patient: Oh, yes, I can sit now and it doesn't bother me.

Dr. Soll: Is there any discomfort at all?

Patient: No, there is just stiffness in my back. Of course the tingling in my toes is still there, but I guess that will improve.

Student doctor: As a child or young lady, were you ever conscious of any pain in your leg or back, or was there any indication that there was something wrong?

Patient: No, not to my knowledge. My mother looked for signs afterward and she noticed that I wore out the sole of my right shoe more. Whether this is significant or not, I don't know.

Dr. Magraw: How close are you to becoming completely well?

Patient: Very close, I hope.

Dr. Magraw: What do you mean, you hope?

Patient: Once the stiffness has gone away I should be well except for taking it easy. I have all my reflexes back. It is good to see them all jump again.

The Patient Exits the Room

Miss **Helen Kretchmer:**[*] There are three small children in the family — aged three, nine and 15. The family lives on a farm which they have been purchasing over a period of time. It is a very modest farm in an area which will become part of the state game reserve. Although the state will probably buy their farm, they will still be able to live on it. In the past they have lived in various parts of the country. The husband built the house they are now living in with his own hands, and I presume that the patient helped a great deal. At the present time the family is cared for by the husband, who takes the smallest child to a babysitter during the day while the other children are in school. When the patient goes home she may need some assistance with heavy work for a while. She has a very well organized family; otherwise they would need a homemaker. The family has only a marginal income. The father's income is fairly modest, about $292.00 per month as a hardware salesman. They are gradually paying for their farm, and any great added expense would be difficult for them. Their hospital bill is already $400.00. In addition to their farm and the father's wages they own a small property in another state which that state wants to buy. This could be liquidated to provide money for them now.

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[*] Supervisor and assistant professor, social service, University of Minnesota Hospitals.

If the mother needed therapy or care in the home, a public nurse could be obtained, as this service is available to anyone in the county regardless of income. The welfare board can provide various kinds of aid, such as assistance to the family through Aid to Dependent Children during the period of disability or payment for hospital care.

Robert W. Soll, M.D.
University of Minnesota
Hospitals

Participating in the conference were: Dr. Lyle A. French, Professor and Director Neurosurgery; Dr. Richard Magraw, Director, Comprehensive Clinic Program; Dr. John Brantner, Assistant Professor Clinical Psychology; Miss Helen Kretchmer, Supervisor and Assistant Professor, Social Service; and Dr. Robert Soll, Neurologist.

Religion Circa 90 A.D.

The following letter written by Pliny is esteemed as a record of ecclesiastical antiquity, written about 40 years after the death of St. Paul.

To the Emperor Trajan:

It is my invariable rule, sir, to refer to you in all matters where I feel doubtful — having never been present at any trials concerning those who profess Christianity, I am unacquainted not only with the nature of their crimes, — but how far it is proper to enter into an examination concerning them. Whether repentence entitles them to a pardon; or if a man has been once a Christian, it avails nothing to desist from his error; whether the very profession of Christianity, unattended with any criminal act, or only the crimes themselves inherent in the profession are punishable; on all these points I am in great doubt. I asked them whether they were Christians; if they admitted it — if they persisted I ordered them to be at once punished: for I was persuaded, whatever the nature of their opinions might be a contumacious and inflexible obstinacy certainly deserved correction — some among those who were accused by a witness in person at first confessed themselves Christians, but immediately after denied it. They all worship your statue and the images of the gods, uttering imprecations* at the same time against the name of Christ. They affirmed the whole of their guilt was that they met honestly today and addressed a prayer to Christ, as to a divinity, binding themselves by a solemn oath, not for the purpose of any wicked design but never to commit any fraud, theft, or adultery, never to falsify their word or deny a trust when they should be called upon to deliver it up. From this custom they desisted after the publication of my edict by which according to your commands I forbade the meeting of any assemblies — all I could discover was evidence of an absurd and extravagant superstition. In fact this contagious superstition is not confined to the cities alone, but has spread its infection among the neighboring villages and country. Nevertheless, it still seems possible to restrain its progress.

Trajan to Pliny:

You have adopted the right course, my dearest secundus — against the Christians who were brought before you. If indeed the crime (of Christianity) is proved they must be punished with the restriction, however, that while the party denies he is a Christian and shall make it evident that he is not, by invoking our gods, let him, not withstanding any former suspicions, be pardoned upon his repentence. Anonymous information ought not to be received in any sort of prosecution. It is introducing a very dangerous precedent and is quite foreign to the spirit of our age.

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*See Test Your Word Score Page 1491.

America is a song. It must be sung together. — Gerald Stanley Lee

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Child Psychiatry

School Failure*

"School failure?" the physician may ask, "What has that to do with me?" The answer is, of course, "Quite a lot if you deal with children and their parents."

Contrary to the expectations of most parents, a significant number of children do fail in school. Whether the child fails academically or whether he fails to make the necessary behavioral adjustment, he is threatened in three ways: (1) He recognizes his own inability to compete successfully; (2) he senses the disappointment of his parents; (3) he loses the acceptance of his peers. Persistent failure builds up the child's concern to the point where his tolerance capacity is exceeded and he seeks a way out. One comfortable way out — because it is acceptable — is illness or the manifestation of symptoms of illness. This is where the discerning physician comes in.

School failures are costly, not only to the individual but to society. The physician has a responsibility to the child, the parents, the school, and the community to recognize danger signals and to apply or recommend preventive measures. If serious failure has already occurred before the physician is consulted, he must ferret out the underlying causes, deal with those within his purview, and enlist the help of other experts when necessary.

Indications of Impending Trouble

The most frequently encountered indications of impending trouble are: (1) an abrupt change of pace in general behavior — increased restlessness, inability to apply self to an assigned task, excessive day dreaming, deterioration in interpersonal relationships; (2) a marked reversal in attitude and disposition — unexplained fearfulness, a tendency to be easily upset, withdrawal from group activity, lack of the usual enjoyment of companionship; (3) a sudden drop in academic performance; (4) persistent offering of physical complaints — headache, stomach ache, fatigue, and the like; (5) exaggeration of or increase in the frequency of asthmatic attacks or convulsive seizures, difficulty in diabetic control; (6) repeated absences from school because of illness; (7) a developing pattern of tardiness and/or truancy; (8) out-and-out refusal to go to school where the child's helplessness is manifested by his saying, "I *can't* go to school," rather than "I *won't*."

The underlying causes of school failure tend to fall into five general categories. They may be present in varying combinations, depending on the child's age and the circumstances of his life. Sometimes the root of his difficulty can be readily diagnosed, but other factors feed the root. The total problem is likely to be complex.

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*In the hope of stimulating further interest in the art of dealing with children and their parents, the editor has agreed to publish a series of papers on subjects of special relevance.

Continued

Academic Potential

Adequate academic potential is essential for school success. When a child is failing, his mental ability obviously should be evaluated. While the services of a competent psychologist are invaluable in measuring the intelligence factor and analyzing its impact, a physician alert to the significance and meaning of developmental norms for any given age group usually can at least estimate the child's general capacity.

Intellectual Level

In terms of academic potential, children can be classified as gifted, superior, average, borderline, and retarded. School failure can occur in any of these groups, though children of average capacity usually fail for other reasons. Marked retardation is easy to spot, but the group falling between the obviously retarded and those classed as "average" is more difficult to define. In general, these borderline children tend to have trouble from the beginning, hovering between passing and failing until the fourth or fifth grade. At this point failure is the rule. Because they are capable of competing successfully with their peer group in all areas of activity except "book learning," their limitation in this respect may have been overlooked. All too often parents and teachers mistakenly expect too much of them. Their inability to live up to such expectations adds another stressful dimension to their failure. The first requirement in cases like this is clarification and acceptance of the reason for unsatisfactory academic performance. The next is a modified program which utilizes their manual skills and enables them to attain reasonable pleasure and satisfaction from school work. Continuing to pass them along in the usual fashion without regard for their limitations only magnifies their frustration and resentment.

Boredom

The superior or gifted child may fail because he does not have sufficient opportunity to utilize his full potential. The curriculum in most school systems is designed for the average child. Early in his school experience the above-average child may get bored. As his boredom and consequent resentments mount, he may become an "acting out" problem. Relieved of the necessity to really apply himself, he may develop poor study habits. Then as he advances and assignments become more difficult, his poor habits take their toll and his achievement is not commensurate with his ability. On the other hand, a different kind of problem may result from advancing the superior or gifted child a grade or two without considering whether he is physically, socially and emotionally mature enough to compete with older children. To avoid complications, the child's capacities to deal successfully with the total range of competition must be assessed, and the child himself should participate in the decision. How he feels about the changes involved in advancement is important.

Experimentation with the ungraded approach, particularly at the elementary level, is an encouraging development. As more schools adopt it, many of the problems related to variations in academic potential may be eliminated.

Physical Disorders

Physical defects may be responsible for school failure. Accurate perception is a first essential in the learning process. Any defect of sight or hearing penalizes the child. Minimal defects are more, rather than less, important, because they are likely to be overlooked. The result is accumulated strain which saps the child's vitality. Early recognition and correction of the defect may avert failure. The child handicapped by poor muscular coordination, and control needs special consideration and encouragement. Speech disorders such as stammering or those related to cleft palate defects likewise may contribute to school maladjustment.

Chronic and acute illnesses take their toll in school failure. Repeated or prolonged absences from school cause the child to get behind in his work and everything looks hopeless. Part-time tutoring during convalescence often is the answer. If a child exhibits general disinterest and lassitude, the possibility of malnutrition with an associated anemia must be considered. Unusual physical features such as tallness or shortness, obesity, or a physical deformity may be indirectly responsible for school failure. Through discussion and reassurance the physician may be able to help the child accept his difference.

Special Disabilities

An obvious prerequisite for successful performance in school is the ability to read satisfactorily, yet estimates suggest that 10-20 per cent of our children are unable to do so. Modern methods of teaching reading account for some of this difficulty. Children who do not respond to the "flash card" system may require intensive work in old-fashioned phonetics. A small, but significant, group have a specific reading and writing disability. These children as a rule are late in establishing — or may never establish — cerebral dominance. They tend to reverse words and letters. For example, they see "saw" for "was" and vice versa, or confuse "b" and "d," "p" and "q." Some are mirror writers and readers, seeing "yod" for "boy." Children of this type encounter trouble in the early grades, and their ability to compete diminishes progressively, though they may do well in subjects which do not require reading. They need intensive help from specially trained individuals.

Inadequate Preparation

Another group of children fail because of inadequate preparation in the fundamentals — reading, writing, spelling and arithmetic. Poor teaching may be responsible, but more often the key to their dilemma lies in a history of changing schools. It is estimated that approximately one third of our population is mobile. Adjustments to varying academic standards, new teachers and different methods, new classmates, and new surroundings are not easy — particularly for the young child. Still another group fails because of inadequate social preparation. A good example is:

Excessive Emotional and Nervous Tension

Emotional disturbances in children are not sufficiently recognized as causes of school failure. They are particularly important when the child begins his school career. From this time on, the responsibility for adjustment rests primarily with him. The attitudes of his teacher, his parents, and his doctor can either help or hinder the adjustment process. Real or imagined fears as well as anxiety — the commonest nervous disturbance

Continued

in both children and adults — may be instrumental in failure. The tactless and unsympathetic teacher, the nagging parent who expects too much of the child, parental discord, or the lack of full acceptance on the part of anyone important to the child can create anxiety. Fear of failure, punishment, criticism, or heckling by fellow students may produce sufficient strain to cause failure. In adolescence tensions may increase with problems centering around emancipation from the home, choosing a life's work, and developing heterosexuality. Wise guidance in these areas may mean the difference between school failure and success. The physician is in a strategic position to offer such guidance, provided he understands and remembers that children need support and encouragement in their struggle to adjust themselves to life as they find it.

Summary

The early diagnosis and management of school failure effects a total saving to the child, the home, the school, and the community. In this the physician can be helpful. Careful search will usually reveal the reason for failure. When this has been determined, a plan of treatment designed to meet the needs of the child can be arranged. For the more complicated cases, referral for specialized help may be desirable. An objective, but sympathetic, interpretation of the child's needs to the parents as well as to the school will do much to reduce the likelihood of school failure and to improve the general health of the school child.

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The Tobacco Tyrant*

Favagoer noted arrhythmia, bradycardia and tachycardia, precordial pain, dyspnea, cardiac asthma, cyanosis, and even Cheyne-Stokes respiration. He reports a fatal case of "Cardiac Paralysis" in which autopsy showed dilatation and fatty degeneration.

Potter's Materia Medica says: "Nicotine is almost as rapidly fatal as Prussic Acid, death having occurred from a toxic dose in three minutes, with no symptoms except a wild stare and a deep sigh. The continued use of tobacco in excess by smoking or chewing produces granular inflammation of the fauces, and pharynx, atrophy of the retina, dyspepsia, lowered sexual power, nervous depression, and occasionally angina pectoris. Used by the young, it hinders the development of the higher nerve centers, and impairs the body nutrition by interfering with the process of digestion and assimilation."

Rolleston says that he has seen two severe cases of anginoid pains, such as substernal oppression and tightness on exertion, and that this is not uncommon in smokers.

Kjelberg believes in a specific psychosis from tobacco. Ziehen and Obersteiner speak of tobacco paralysis.

To be continued next issue.

E. O. Giere, M.D.**
Minneapolis, Minnesota

**Editor's Note: In 1928 Dr. E. O. Giere, M.D. prepared and presented a manuscript at one of the Twin City hospitals on the evil effects of tobacco.*

Through the courtesy of his sons, Doctors Richard and Joe Giere, the timeworn and faded manuscript was made available to the editor. Excerpts will be printed serially.

See Minnesota Med 48:1376, 1965.

Clinical Path Conference

Pathology of Sudden Death*

When a physician is called upon to minister to a person who has "just died" or one who has suddenly developed a state of extremis, planning and execution of resuscitative measures must be pertinent to the condition at hand. Under the dramatic circumstances considered, an exact diagnosis of the basic problem cannot always be made; but it is helpful for the physician to have an awareness of the potential of the problems with which he is faced. Such an awareness may be derived from knowledge of the conditions which may cause sudden death. It is the purpose of this report to review these conditions.

Sudden death, as used in this presentation, is defined as a nontraumatic phenomenon in which, following a stable state, the subject either instantaneously or after a brief episode of discomfort loses all vital functions. Sudden death results from failure of the (1) nervous, (2) respiratory or (3) circulatory system from a variety of causes and mechanisms (Table 1).

TABLE I

Classification of Lesions Responsible for Sudden Death

- I. Nervous System.
- II. Respiratory System.
- III. Circulatory System.
    - A. Myocardial Failure.
        - 1. Fatal arrhythmia.
            - a. Coronary atherosclerosis.
            - b. Left ventricular hypertrophy.
            - c. Left ventricular outflow obstruction; aortic insufficiency.
            - d. Complete heart block.
            - e. Acute myocarditis.
        - 2. Sudden strain upon left ventricle.
            - a. Acutely developing shunt.
            - b. Acutely developing valvular insufficiency.
    - B. Cardiac Compression; Hemopericardium.
        - 1. Rupture of the heart.
        - 2. Dissecting aneurysm of the aorta.
        - 3. Dilatation of the aorta.
    - C. Hemorrhage.
    - D. Obstruction of Valves or Pulmonary Vessels.
        - 1. Acute pulmonary embolism.
        - 2. Chronic pulmonary vascular obstruction.
        - 3. Valvular occlusion.

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*Study supported by Research Grant HE-5694 of the National Institute of Health, United States Public Health Service.

Continued

I-Nervous System

Only rarely do acute lesions of the central nervous system cause sudden death, as in most instances, regardless of how extensive the lesion, the subject maintains circulatory and respiratory functions for several hours at least. In a rare instance of infratentorial hemorrhage, such as rupture of an aneurysm of the circle of Willis, will death from a lesion of the nervous system be sudden.

II-Respiratory System

Respiratory disturbances that cause sudden death are usually those resulting from lodgement of a foreign body in the major airway. Included in this category is the phenomenon in adults of aspiration of a large bolus of food such as a piece of inadequately chewed meat. In children, respiratory failure that leads to sudden death is at times identified as resulting from aspiration of a foreign body. The so-called "crib death," a circumstance in which a seemingly healthy infant is found dead, may result from one of many causes. Recognized respiratory lesions include pneumonia and bronchitis, but in many of such subjects no significant lesion is demonstrable.

In adults respiratory failure may result from aspiration of blood from rupture of a major arterial vessel into the airways. Included among underlying lesions are (1) aneurysm of the thoracic aorta, (2) postradiation necrosis of a carotid artery and (3) mycotic aneurysm of a pulmonary artery.

III-Circulatory System

Collectively, circulation disturbances constitute the most common cause

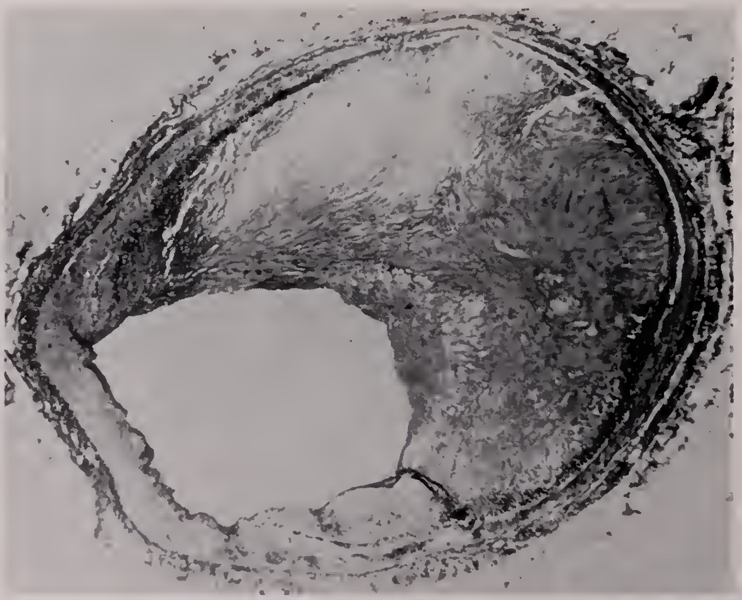


Fig. 1 — Photomicrograph of a coronary artery showing the typical lesion of atherosclerosis. This lesion represents the underlying factor in the majority of cases of sudden death among the population of this country. Elastic tissue stain; x40.

for sudden death. These may be subdivided into four major groups as follows: (1) myocardial failure, (2) cardiac compression, (3) hemorrhage and (4) circulatory obstruction.

Myocardial Failure

Myocardial failure may be subdivided into that resulting from (1) an arrhythmia and (2) sudden strain upon the left ventricle.

Fatal Arrhythmia

An arrhythmia which distorts the circulatory system to the degree that it causes sudden death takes the form either of ventricular fibrillation or cardiac standstill. These two arrhythmias collectively may be called fatal arrhythmias and constitute the most common cause of sudden death.

(a). Coronary Atherosclerosis

Among the many background diseases responsible for a fatal arrhythmia, coronary atherosclerosis stands out as the most prevalent (Figure 1). In the study of Spiekerman and others in Rochester, Minnesota, with which the author was associated,[1] the incidence and types of coronary deaths among residents of that community were determined. Representing a necropsy percentage of about 67 of all deaths occurring in and out of hospitals over a six-year period, the study included 691 necropsies of subjects 20 years of age or older. In this group there were 221 deaths attributable, in one way or another, to coronary atherosclerosis. This represented 41 per cent of the 373 males and 22 per cent of the 318 females in the study. Significant was the fact that the most common single type of death (as determined from history and necropsy findings) was sudden death considered to have resulted from a fatal arrhythmia without acute myocardial infarction. This factor was regarded as operative in 94 subjects, constituting 43 per cent of all coronary deaths. This figure was slightly

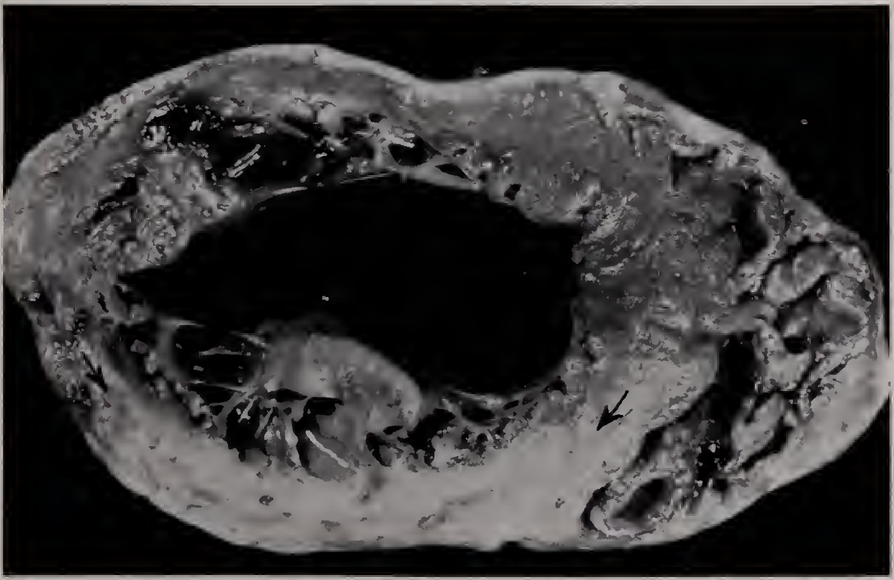


Fig. 2 — Cross section of ventricles of the heart in an instance of healed anterior and acute posterior (between arrows) myocardial infarction. In instances of acute myocardial infarction sudden death is often the result of acute changes in the function of the viable muscle around the infarct rather than changes in the infarct itself.

Continued

higher than the incidence of death associated with acute myocardial infarction which occurred in 87 subjects or 39 per cent of the coronary deaths. Moreover, the high incidence of an arrhythmia leading to sudden death among coronary fatalities was enhanced by the fact that in 20 of the 87 subjects dying with acute myocardial infarction the mechanism of death appeared to be the development of a fatal arrhythmia (Figure 2). Combining the 94 cases of sudden death without acute myocardial infarction and the 20 cases of sudden death with acute myocardial infarction there resulted 114 cases among the 221 coronary deaths in which a coronary death appeared to have resulted from an arrhythmia.

From Tables 2 and 3 it is evident that the majority of subjects dying suddenly of coronary disease are (1) out of hospital and (2) do not suffer from acute myocardial infarction. Scars of healed myocardial infarction are common among such subjects.

TABLE 2
Myocardial Changes in 114 Instances of Sudden Death of Coronary Origin. Modified from Spiekerman and Associates[1]

Condition	Per cent
Normal Myocardium	12
Healed Infarction	70
(Gross)	(42)
(Patchy)	(28)
Acute Infarction	9
Acute and Healed Infarction	9
Total	100

TABLE 3
Location of 114 Subjects Dying Suddenly from Coronary Arterial Disease. Modified from Spiekerman and Associates[1]

Place	Number of Cases	Per cent
Home	77 (65 slight to moderate activity; 12 asleep)	67
In public place	10	9
At work	9	8
In hospital	18	16
Total	114	100

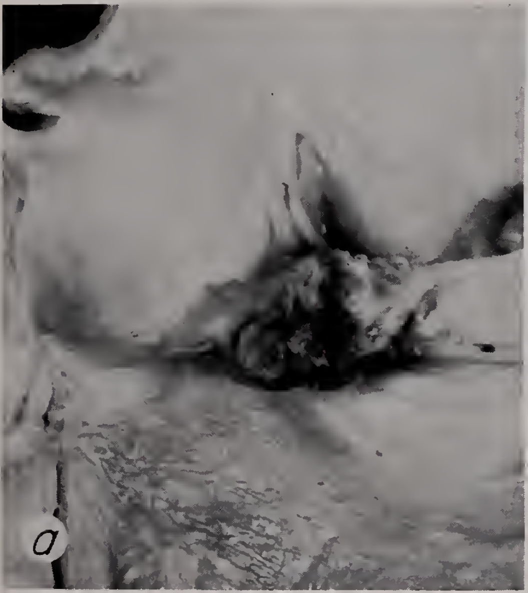
It is of further interest to review the causes of death among patients with scars of healed myocardial infarcts, as these represent examples of patients who had recovered from acute myocardial infarction. The combined studies of Achor and associates[2] and of Juergens and associates[3] yield 329 cases of necropsy-proved healed myocardial infarction. Two thirds of these subjects died of causes related to the coronary arteries.

These causes could be grouped into three categories as follows: (1) sudden death, (2) circumstances related to recurrent acute myocardial infarction and (3) congestive cardiac failure. Of these three groups sudden death was the largest, being represented by 38 per cent of the subjects with healed myocardial infarction who died of coronary disease. In the combined studies to which reference was made, recurrent acute myocardial infarction was observed in 34.5 per cent of coronary deaths and congestive cardiac failure in 27.5 per cent.

A relatively unusual type of acute coronary insufficiency is that resulting from coronary embolism. Sources for such a process included bacterial endocarditis (Figure 3), particles from a calcified aortic valve, left atrial myxoma, mural thrombi of the left atrium or ventricle, and bronchogenic carcinoma that has invaded a pulmonary vein.

(b). Left Ventricular Hypertrophy

It may be taken as axiomatic that the hypertrophied left ventricle (Figure 4) represents a hazard (including the possibility of sudden death)



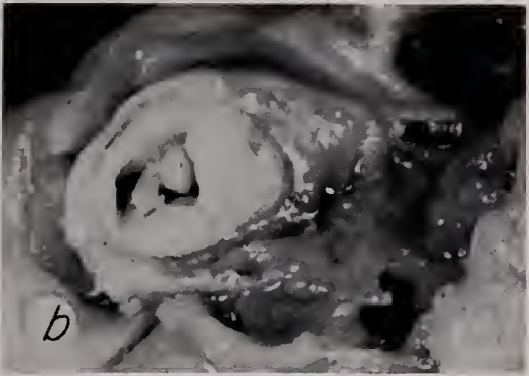


Fig. 3 — Bacterial endocarditis and coronary embolism in a 49-year-old man who died suddenly. *(a)* Segment of the aortic valve in which two leaflets are interadherent. At the zone of adhesion a vegetation of bacterial endocarditis is present. *(b)* Cross-section of the anterior descending coronary artery showing an embolus occluding the lumen, a process considered to have been the basis for sudden death.

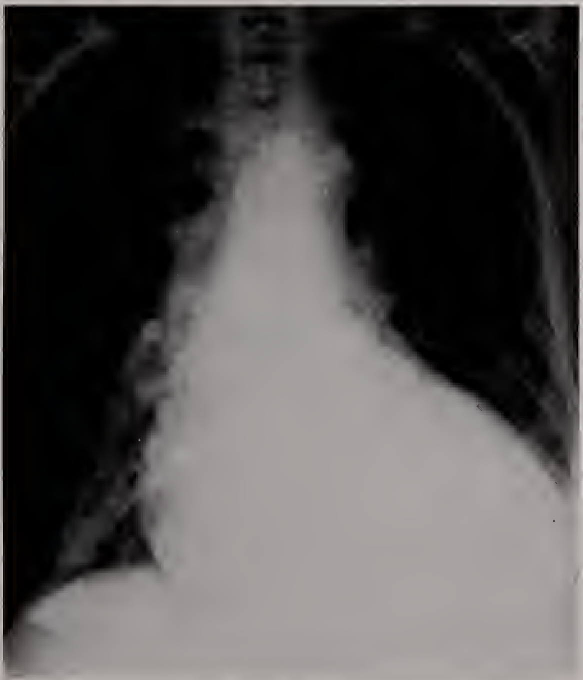


Fig. 4 — Roentgenogram of thorax of a patient with aortic valvular disease showing features of left ventricular enlargement. The left ventricular enlargement, of itself, may be a basis for sudden death.

Continued

to the patient, regardless of the cause of the hypertrophy. In the majority of cases the basis for the left ventricular hypertrophy is evident, frequently taking the form of aortic valvular disease. In other instances one observes examples of sudden death with left ventricular hypertrophy after the basis for the left ventricular hypertrophy, such as coarctation of the aorta, aortic valvular disease or patent ductus arteriosus, has been surgically corrected. The cause of sudden death in instances of left ventricular hypertrophy may perhaps be related to myocardial ischemia resulting from the hypertrophied muscle causing an inordinately high degree of resistance to capillary flow.

Obstruction to left ventricular outflow constitutes a particularly common cause of left ventricular hypertrophy and of sudden death. Special consideration needs to be given to this subject.

(c). Left Ventricular Outflow Obstruction; Aortic Insufficiency

Three anatomic states are responsible for obstruction to left ventricular outflow (Figure 5). In order of decreasing frequency these are (1) aortic stenosis, (2) subaortic stenosis and (3) stenosis of the ascending aorta (supravalvular aortic stenosis). As the subjects of aortic valvular stenosis and aortic insufficiency are each closely related to the subject of sudden death, these will be considered together.

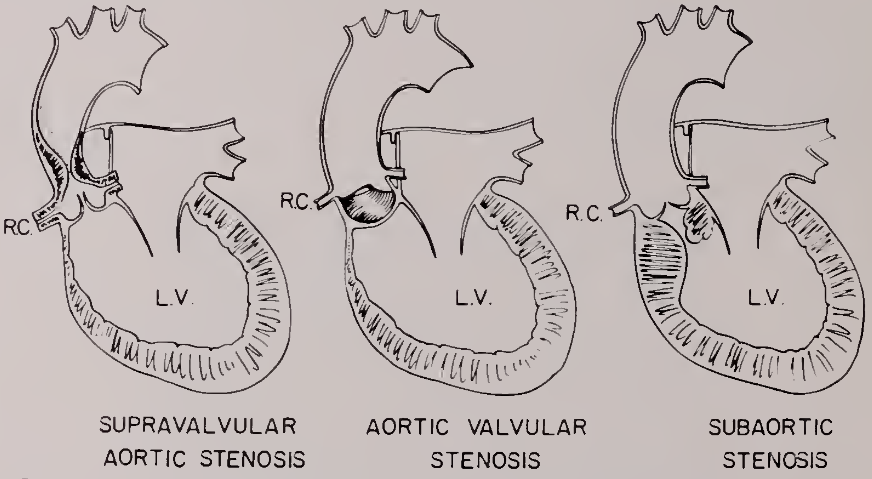


Fig. 5 — Types of obstruction to left ventricular outflow in relation to the aortic valve. These are supravalvular aortic stenosis, aortic valvular stenosis and subaortic stenosis. Each of these types may be associated with sudden death. Illustration from Edwards.[11] Reproduced with permission from the American Heart Association.

Among patients dying with aortic valvular disease, whether the disease takes the form of stenosis or of insufficiency, sudden death is common (Figure 6). In a series of 36 inhospital nonsurgical adult patients dying with aortic valvular disease, Nakib and associates[4] found that sudden death had occurred in 12 of the cases (33 per cent).

In some of these subjects coronary atherosclerosis was present to the degree that is commonly found among individuals dying suddenly of coronary disease without aortic valvular disease. In such subjects it is impossible to determine whether the aortic valvular disease or the coronary atherosclerosis was at fault. Nevertheless, in some of the subjects of Nakib, as in cases of other series in which sudden death was associated with aortic valvular disease, coronary atherosclerosis was present to only a mild and nonsignificant degree.

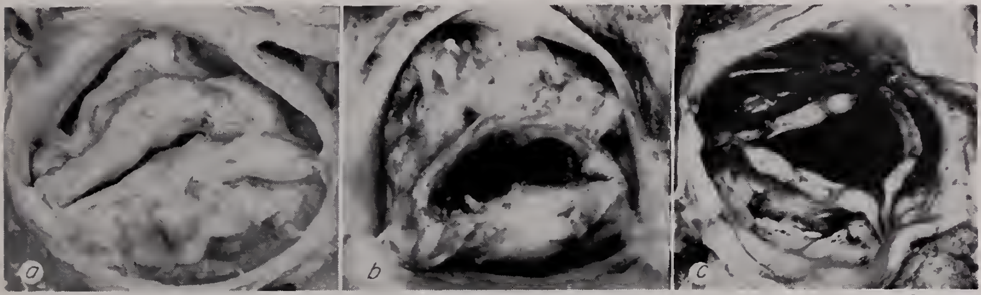


Fig. 6 — Types of aortic valvular disease which may be responsible for sudden death. *(a)* A congenital bicuspid aortic valve with acquired calcification yielding a stenotic valve. From a 65-year-old woman. *(b)* In a 43-year-old woman, a congenital bicuspid aortic valve which is calcified and stenotic. Coexistent retraction of the cusps causes the valve also to be incompetent. *(c)* Rheumatic aortic valvular insufficiency from a 25-year-old woman who died suddenly. Characteristic thickening and retraction of aortic leaflets leaving an incompletely guarded orifice.

The sudden death that results from aortic valvular disease is probably to be attributed to an arrhythmia associated with ischemia. Uncertain, however, is whether the ischemia is a direct result of the peculiar hemodynamic changes of aortic valvular disease or whether it is a result of the nonspecific problem of the associated left ventricular hypertrophy.

Special mention should be made of the problem of congenital aortic valvular stenosis. It is recognized that in infants or children with symptomatic aortic stenosis sudden death is commonly observed.

The other two types of obstruction to left ventricular outflow are subaortic stenosis and supravalvular aortic stenosis. With either of these conditions the patient may live to adult life but the danger of sudden death is ever present. In supravalvular aortic stenosis the tendency for premature development of coronary arterial obstructive lesions[5] may be an additional factor predisposing to sudden death.

(d). Complete Heart Block

Complete heart block in which Adams-Stokes attacks are classically associated has a strong tendency to cause sudden death, either through the development of ventricular fibrillation or cardiac standstill. In some patients the basis for complete heart block is clearly identifiiable, while in others its cause remains obscure. Identifiable causes include (1) surgical injury to the bundle of His during closure of a ventricular septal defect (Figure 7) or placement of a prosthetic aortic valve, (2) infiltration of the bundle of His by tumor, amyloid or inflammatory exudate, (3) congenital discontinuity of the major conduction pathways or (4) infarction of the bundle of His.

Heart block developing spontaneously in subjects over 60 years of age frequently is without a clear-cut anatomic basis. Moreover, the tendency for this disturbance to exhibit periodic variation in degree supports the view that continuity of the conduction tissue is maintained and that the problem is one of varying degrees of resistance to conduction, perhaps from ischemic or biochemical causes.

(e). Acute Myocarditis

Acute myocarditis may become complicated by sudden death. In some

Continued

subjects one may demonstrate necrosis and an inflammatory reaction in the bundle of His and clinically complete heart block may have been identified. In other subjects no major lesion of the conduction tissue is identifiable while ventricular extrasystolic beats may have been identified. Such beats may perhaps be taken as evidence for hyper-irritability of the myocardium and one may then infer further that this tendency may set the stage for ventricular fibrillation.

Sudden Strain Upon Left Ventricle

Sudden death may follow a state in which an acute load is placed upon the left ventricle. Under this category are two groups of conditions: (1) an acutely developing shunt and (2) acute valvular insufficiency.

(a). Acutely Developing Shunt

Shunts that develop acutely may be entirely or partially intracardiac or they may be extracardiac. For any given type some patients maintain sufficient cardiovascular efficiency to sustain life for weeks, months or even longer. In other subjects the same anatomic state results in death within minutes after its development.

The major completely intracardiac shunt is rupture of the ventricular septum occurring as a complication of acute myocardial infarction, usually in a posterior location.[6,7] In those patients who deteriorate dramatically from the newly developed interventricular communication, pulmonary edema and death occur rapidly in that order.

The classical partially intracardiac shunt which develops acutely is rupture of an aneurysm of an aortic sinus into a right-sided cardiac

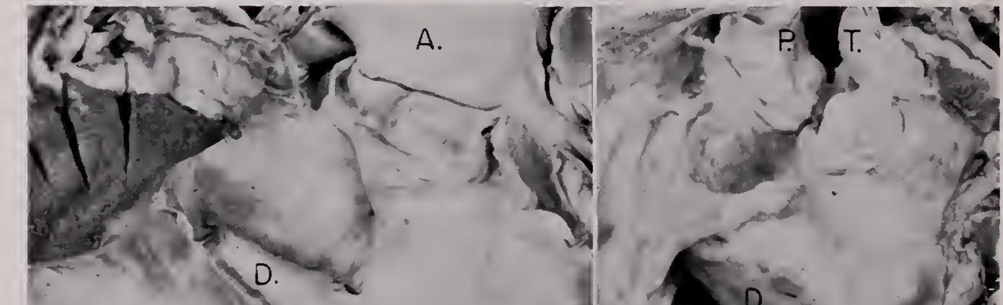


Fig. 7 — Specimen of heart from a 23-year-old man who developed complete heart block from closure of a ventricular septal defect. Sudden death occurred two months postoperatively. *(a)* Left ventricular (L. V.) aspect and ascending aorta (A.). Beneath the aortic valve is the site of the closed ventricular septal defect (D.). *(b)* Right ventricle (R. V.) and pulmonary trunk (P. T.). The site of closure of the ventricular septal defect with a prosthetic patch (D.) is evident. The prosthetic patch is, in part, encased by fibrous tissue.

chamber (Figure 8). Most commonly, the aneurysm is of the congenital variety and is not associated with evidence of cardiovascular disease until the dramatic event of rupture of the aneurysm. In a lesser number of cases the aortic aneurysm is of the mycotic type, being a complication of bacterial endocarditis.

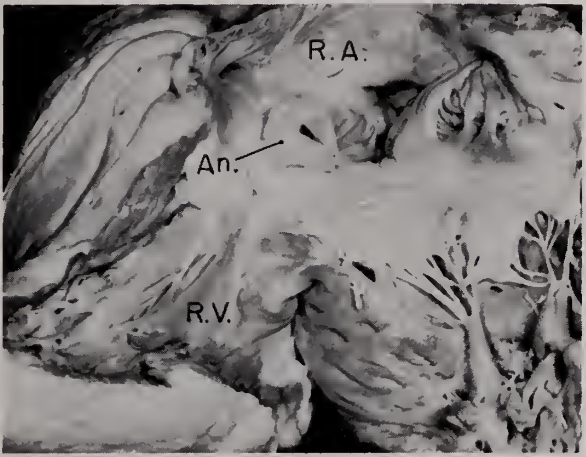


Fig. 8 — Rupture of an aortic sinus aneurysm into the right atrium. The aneurysm (An.) protrudes into the right atrium (R. A.) above the tricuspid valve. A laceration is present in the center of the aneurysm. R. V. = right ventricle. From a 45-year-old man who died suddenly.

The entirely extracardiac shunts that develop acutely are usually complications of syphilitic aortitis. In this circumstance either a uniformly dilated ascending aorta or a saccular aneurysm of the ascending aorta ruptures into an adjacent vessel such as the superior vena cava (Figure 9*a*) or a pulmonary artery (Figure 9*b*).

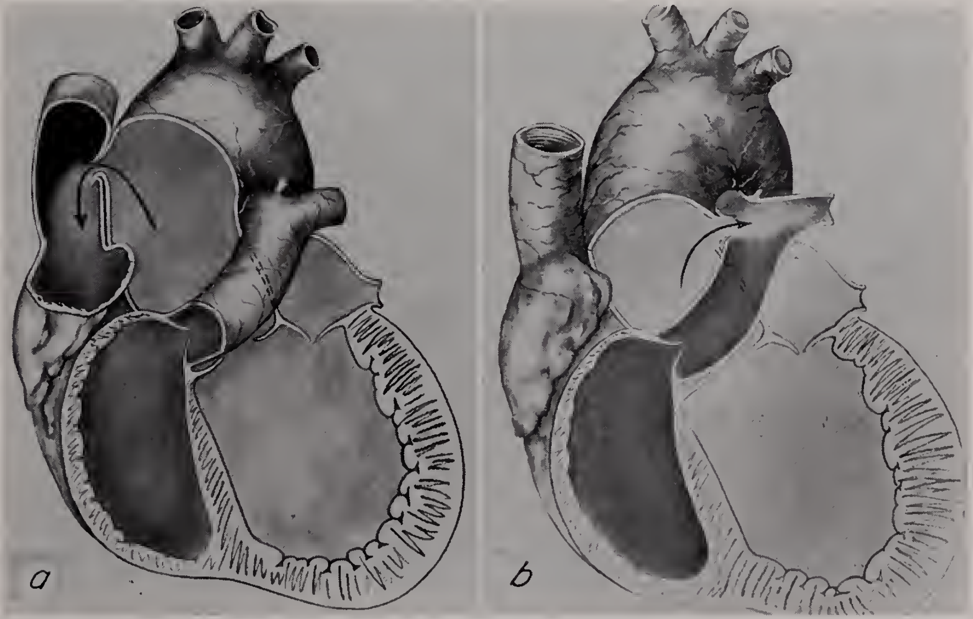


Fig. 9 — Diagrammatic portrayal of acquired shunts which may be responsible for sudden death. *(a)* Syphilitic aortitis with rupture of the aorta into the superior vena cava. *(b)* Syphilitic aortitis with rupture of the ascending aorta into the pulmonary arterial system.

Continued

As with ruptures of the ventricular septum or of an aortic sinus aneurysm, the appearance of an extracardiac shunt may be followed either by sudden death or by a state of sufficient cardiovascular stability as to maintain life for some time.

(b). Acutely Developing Valvular Insufficiency

As with acutely developing shunts the course of the individual patient with acutely developing valvular insufficiency may vary from a state of acute pulmonary edema and death within a few minutes to one of chronic cardiac decompensation.

When sudden death complicates acutely developing valvular insufficiency the valve involved is either the aortic or mitral.

Lesions of the mitral valve which pertain to the subject of this communication occupy two major categories as follows: (1) rupture of a papillary muscle complicating myocardial infarction or (2) rupture of chordae tendineae.

Rupture of a papillary muscle usually involves the posteromedial muscle of the left ventricle (Figure 10). The basic myocardial infarct is posterior or posterolateral in location.[8,9] In most instances of this least common type of rupture of the heart, the entire posteromedial papillary muscle loses its continuity. As a consequence, about half of the chordal support of the mitral valve is lost and the resulting mitral insufficiency is of gross proportion.

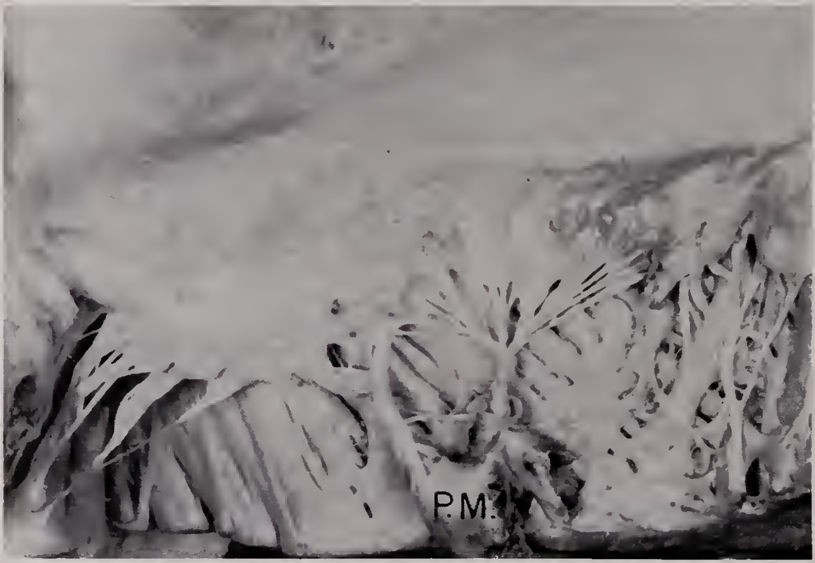


Fig. 10 — Rupture of the posterior papillary muscle (P. M.) in a man aged 53 years with acute myocardial infarction. Following rupture of the papillary muscle that part attached to the chordae had spun through a loop of the chordae to account for the twisted arrangements evident in the chordae. The loss of support of the mitral valve was responsible for acute massive mitral insufficiency.

Rupture of chordae tendineae, to be distinguished from rupture of a papillary muscle, may complicate bacterial endocarditis. More commonly, no underlying inflammatory process is identifiable.

Nontraumatic lesions which cause acute aortic valvular insufficiency primarily may involve either the aortic valve or the ascending aorta.

Within the sphere of the present discussion, primary lesions of the aortic valve are usually destructive complications of bacterial endocarditis. Lesions of the aorta which cause aortic valvular insufficiency involve a laceration of the aorta, as in dissecting aneurysm, a process which may cause either distortion of the aortic root or gross loss of support of part of the aortic valvular structure. In a rare case observed by the author an adult male patient exhibited a zone of avulsion from the aortic wall of the site of attachment of two aortic cusps (Figure 11). The basis for this peculiar nontraumatic avulsion is as yet not explained.

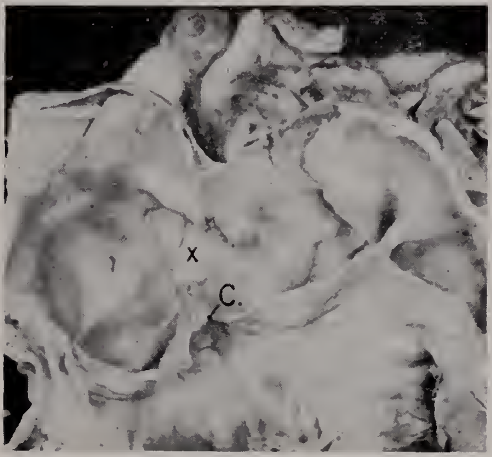


Fig. 11 — Aortic valve and a portion of ascending aorta in a 43-year-old man who died of hemopericardium from rupture of a dissecting aneurysm of the aorta. The commissure between the right and posterior aortic cusps (C.) had become avulsed from its attachment to the aortic wall as point x. Although this lesion had been present for some time before the dissecting aneurysm, it is conceivable that acute death could be caused from such sudden loss of aortic valvular support.

Cardiac Compression; Hemopericardium

Among the several varieties of pericardial disease causing cardiac compression (tamponade), hemopericardium is the one most likely to cause sudden death. Moreover, the accumulation of gross blood in the pericardial sac rarely allows the patient to survive for more than minutes. The great tendency for hemopericardium to cause sudden death stands in contrast to the consequence of an acutely developing valvular insufficiency or of a shunt. With the latter conditions, as has been suggested, while death may occur suddenly, many subjects survive for varying periods of time as examples of chronic cardiac disability.

There are two predominant causes of hemopericardium, namely myocardial infarction and rupture of the intrapericardial segment of the ascending aorta. Myocardial infarction which contributes to hemopericardium is always transmural in type. It occurs either through rupture of the free wall or by way of hemorrhage from associated pericarditis.

Rupture of the Heart

Rupture of the heart may be represented by rupture of a papillary muscle or by rupture of the ventricular septum, two lesions that have been considered in a foregoing section; but the most common type is that in which the rupture is through the free wall of the left ventricle, allowing left ventricular blood to escape into the pericardial sac. There are several features of rupture of the heart that are worthy of mention in addition to the fact that the type of infarct which becomes so complicated is transmural. There is a greater tendency for this complication to occur in women than in men. Of all patients dying with acute myocardial infarction rupture of the heart (usually of the free wall) occurs in about 15 per cent.

Continued

This figure is derived from the fact that of women dying with acute myocardial infarction about 30 per cent have suffered rupture of the heart, while in men dying of acute myocardial infarction about 8 per cent exhibit rupture of the heart. Rupture does not occur through scarred myocardial segments, and rupture of chronic cardiac aneurysms is essentially a nonexistent entity.

The tear itself tends to occur at the periphery of the infarct where paradoxical movement occurs during systole, the living muscle contracting while the infarcted muscle is stretched. After the primary laceration on this mechanical basis, blood dissects through the myocardium and epicardium and into the pericardial cavity (Figure 12).

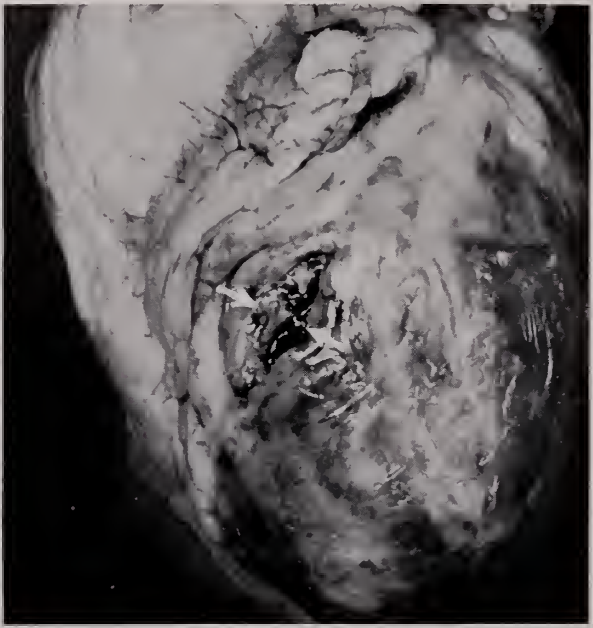


Fig. 12 — Exterior of anterior view of heart in a 65-year-old man with acute myocardial infarction. Rupture (between arrows) through the free wall of the left ventricle led to sudden death from acute cardiac tamponade.

In cases of transmural myocardial infarction *fibrinous pericarditis* may either overlie the zone of infarction or involve the pericardium diffusely. The vascular granulation tissue which participates in organizing the pericardial fibrin may bleed into the pericardial sac, the bleeding varying in amount and in rate of development. In extreme cases signs of acute cardiac tamponade may develop and result in sudden death. It is probably true that the tendency for a hemorrhagic pericardial effusion is greater among anticoagulated than among nonanticoagulated patients, but the fact remains that some nonanticoagulated patients with transmural myocardial infarction may suffer from acute hemorrhagic pericardial effusion on the basis of pericarditis.

Dissecting Aneurysm of the Aorta

Dissecting aneurysm of the aorta stands second only to rupture of the heart as a cause of nontraumatic hemopericardium. This condition occurs either in hypertensive subjects or in normotensive individuals with extreme degrees of idiopathic cystic medial necrosis of the aorta (Figure 13).

Some of the latter subjects show other physical signs of arachnodactyly* (Marfan's syndrome), while others do not.

In dissecting aneurysm of the aorta if external rupture of the aorta occurs, its site depends upon the site of the internal tear, as the two are closely related geographically. It follows that when a dissecting aneurysm of the aorta is responsible for hemopericardium the internal tear is usually in the ascending aorta. This is the same type of dissecting aneurysm in which the intramural hematoma may compress a coronary artery and in that way represent yet another basis for sudden death among subjects with dissecting aneurysm.

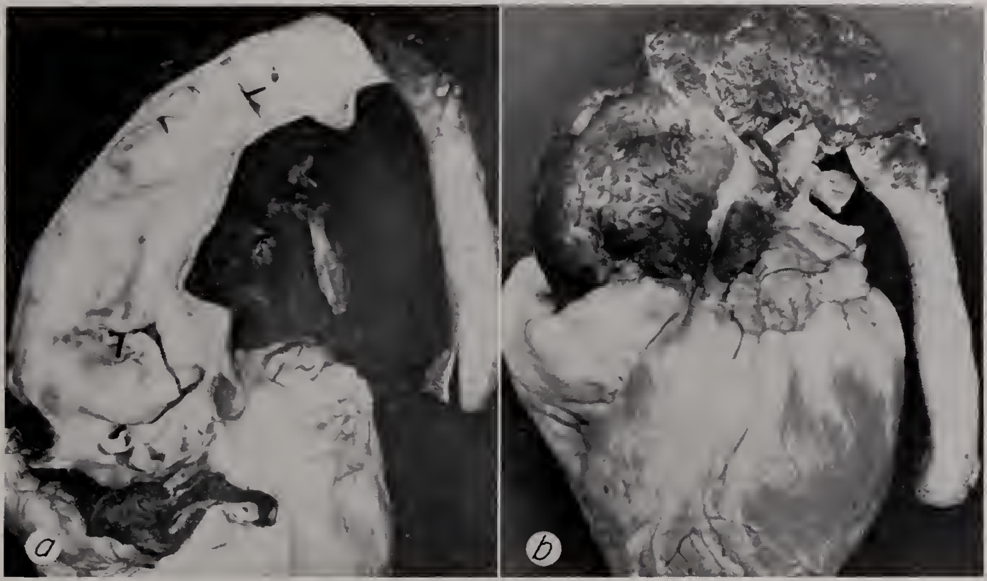


Fig. 13 — Hemopericardium resulting from dissecting aneurysm of the aorta in a 13-year-old boy with Marfan's syndrome. *(a)* The interior of ascending aorta and aortic arch. The rent, in relation to the lower probe, represents the primary internal tear of the dissecting aneurysm, while the rent at the upper probe represents a zone of "re-entry" of the false passage into the aortic lumen. Hemopericardium resulted from external rupture into the pericardial sac. *(b)* Exterior of heart and of thoracic aorta. The aorta adventitia is grossly distended with blood. Below the pericardial reflection a channel led into the pericardial sac and accounted for the acutely developing hemopericardium, which in turn led to sudden death.

Dilatation of Aorta

A less common cause of hemopericardium than myocardial infarction or dissecting aneurysm of the aorta is uniform aortic dilatation with rupture. Background conditions for aortic dilatation include syphilitic aortitis (Figure 14*a*), idiopathic cystic medial necrosis, and senile dilatation of the aorta (Figure 14*b*).

Hemorrhage

When rupture of a major artery is responsible for sudden death, the mechanism is usually one of mechanical interference with a vital structure by the resulting hemorrhage. The hemorrhage may compress the brain stem as in subtentorial hemorrhage. Reference to cardiac compression from hemorrhage has been made.

When bleeding occurs into a major airway the hemorrhage is responsible for asphyxia. Although simple exsanguination may cause sudden death, simple bleeding is usually associated with a recognized state of shock before death ensues.

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*See Test Your Word Score Page 1491.

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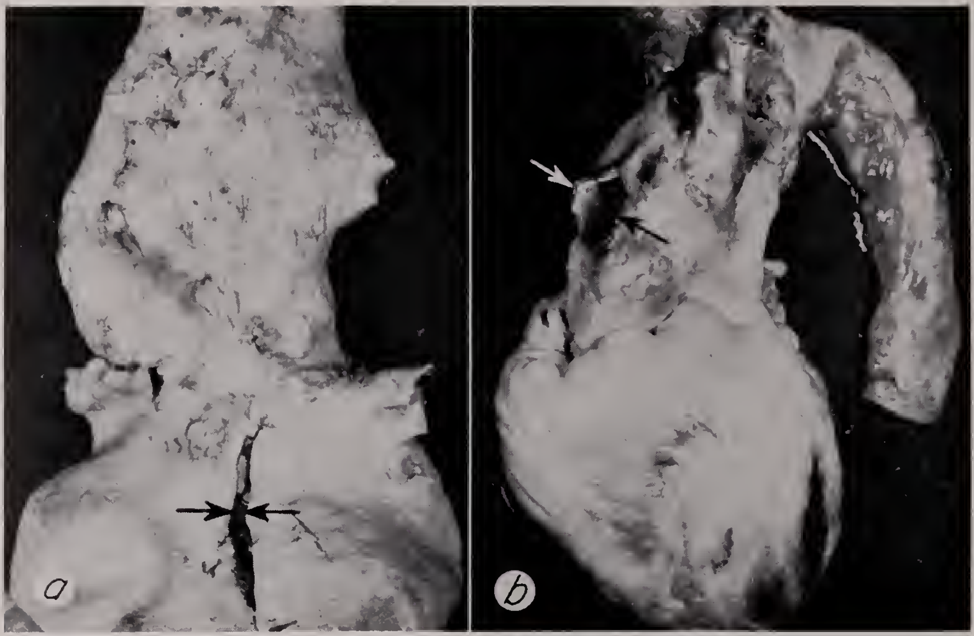

Fig. 14 — Dilatation of aorta with rupture leading to hemopericardium. *(a)* In a 72-year-old woman with syphilitic aortitis the aorta is dilated but not locally aneurysmal. A linear rent (between arrows) of the aorta led to hemopericardium. *(b)* In an 85-year-old woman with senile dilatation of the aorta, gross rupture (between arrows) of the ascending aorta led to hemopericardium and sudden death.

Obstruction of Valves of Pulmonary Vessels

Obstruction of the circulation sufficiently severe to cause sudden death takes several forms. These are (1) acute pulmonary embolism, (2) chronic pulmonary vascular obstruction and (3) valvular occlusion.

Acute Pulmonary Embolism

The most common type of pulmonary embolism is that in which the embolic material is represented by a noninfected thrombus. Important backgrounds for massive pulmonary embolism include cardiac failure or a surgical procedure, the latter particularly of an abdominal nature for malignant tumor. It is, however, to be recalled that a program of bed rest for almost any condition, including so simple a condition as acute respiratory infection, has at times become complicated by acute massive pulmonary embolism. The almost universal source for massive pulmonary embolism is the venous system of the lower extremities, even in cases of cardiac failure with right atrial mural thrombosis. Moreover, a point of significance is that venous thrombosis leading to pulmonary embolism need not be associated with obvious edema of either lower extremity.

In addition to the classic gross pulmonary embolism of bland thrombotic material there are instances of sudden death from unusual types of pulmonary embolism. These include embolism of gross masses of neoplastic tissue originating in the renal vein of a kidney with primary carcinoma. This event is most likely to occur when the kidney is manipulated surgically.

There is yet another form of embolism to the lungs of neoplastic tissue. This involves dissemination of small particles of tumor tissue into small pulmonary arteries and arterioles from a tumor which has invaded a vein. This type of spread is classically associated with a chronic state of pulmonary vascular obstruction,[10] but in an unusual instance the spread may be so extensive at one time as to be followed by death shortly after the event.

Embolism to the lungs of amniotic contents is recognized as a cause of sudden death in instances of difficult labor.

Chronic Pulmonary Vascular Obstruction

Sudden death is universally recognized as a consequence of acute pulmonary embolism. It should also be emphasized that sudden death may occur in instances of chronic pulmonary vascular obstruction, from whatever cause. Included in these are the pulmonary arterial obstruction that may complicate certain congenital anomalies such as septal defects or patent ductus arteriosus with pulmonary hypertension (Figure 15). The mechanism through which sudden death occurs under these circumstances is not clear but may represent acute right ventricular failure in the face of severe obstruction to ejection of blood from this chamber.

Mitral stenosis should be included in the broad category of chronic pulmonary vascular obstruction. In this condition sudden death may, perhaps, at times occur on the simple basis of pulmonary vascular obstruction. Usually, however, death occurring acutely in mitral stenosis is preceded by development of pulmonary edema.

Valvular Occlusion

A dramatic phenomenon is acute occlusion of a valvular orifice. It is hypothetically possible for such an event to involve any of the cardiac valves, but as a rule the mitral valve is the one affected.

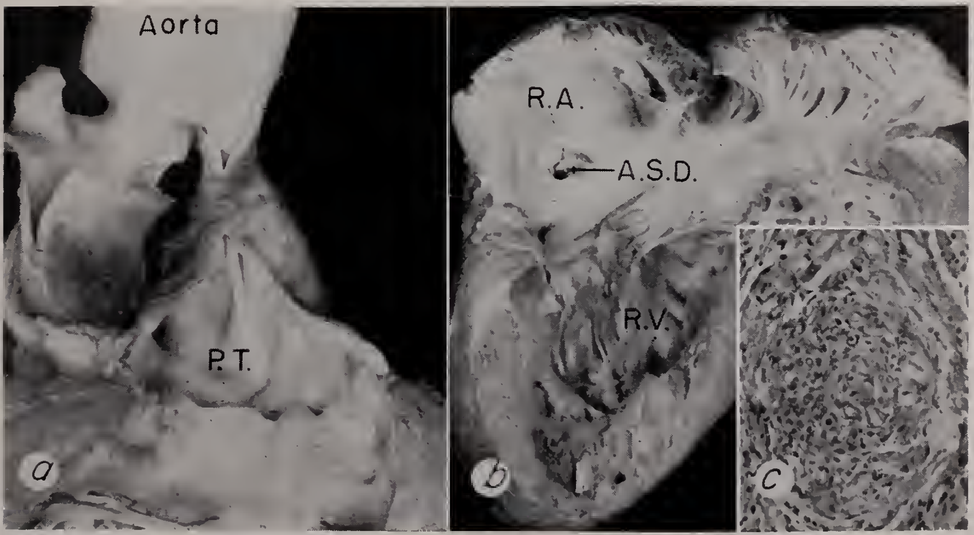

Fig. 15 — Patent ductus arteriosus with pulmonary hypertension in a 7-year-old boy who died suddenly. *(a)* The aorta and pulmonary arterial vessels (P. T.) are connected through a patent ductus arteriosus (containing probe). *(b)* Right atrium (R. A.) and right ventricle (R. V.). A small atrial septal defect (A. S. D.) is present. This may have been insignificant compared to the effects of the associated patent ductus arteriosus. The right ventricular hypertrophy is considered a sign of elevated pulmonary arterial pressure. *(c)* Photomicrograph of a small muscular artery of the lung. Characteristic plexiform lesion occludes lumen. This change is a characteristic of chronic elevated pulmonary arterial pressure. H & E; x200.

Continued

Two background conditions for this phenomenon exist. The first is mitral stenosis in which a left atrial thrombus occludes the valvular orifice. Classically, the thrombus has become detached from its zone of formation and lies free in the left atrium, a condition commonly called a ball valve thrombus. In uncommon instances of mitral stenosis a pedunculated thrombus may be so oriented as to be capable of occluding the mitral orifice.

The second condition which may occlude the mitral valve is the pedunculated left atrial myxoma (Figure 16). We have observed an instance of right atrial myxoma which obstructed the tricuspid orifice and caused a chronic impediment to the flow of blood through this valve. On hypothetical grounds, such a mass could cause sudden death by sudden occlusion of the valvular orifice.

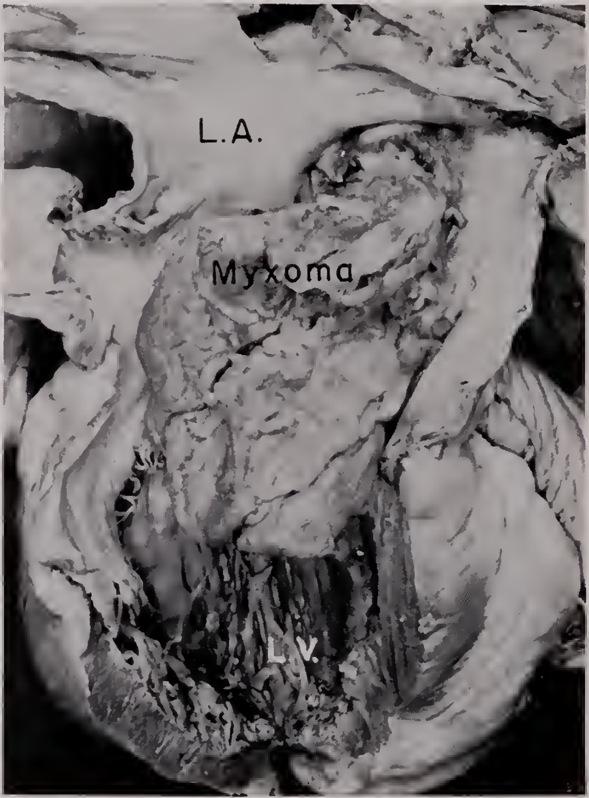

Fig. 16 — Myxoma of the left atrium occluding mitral valve in a 13-year-old girl. The myxoma is attached to the left atrial wall (L. A.) by a pedicle. The tumor engages and occludes the mitral orifice and was responsible for sudden death. L. V. = left ventricle.

In instances of sudden death from occlusion of a valvular orifice by a mass, a history of fainting spells is commonly obtained. This phenomenon is probably explained by the tendency for masses which occlude a valve to do so intermittently.

Summary

Sudden death may be caused by lesions involving the nervous, respiratory or circulatory systems. Lesions of the circulatory system numerically represent the largest group of conditions that may be responsible for sudden death.

Those processes of the circulatory system which may cause sudden death may be subdivided into the following four categories: (1) myocardial failure, (2) cardiac compression, (3) hemorrhage, (4) obstruction. The most common single basis for sudden death is that of myocardial failure which, in turn, is most often brought about by an arrhythmia in individuals with coronary atherosclerosis.

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The Penalty of Overweight

In obesity, because of the increased work of breathing, the oxygen demand is greatly increased, so that respiration may not only be labored, but it may be inadequate and unable to support proper gaseous exchange in the lungs. Consequences may be serious.

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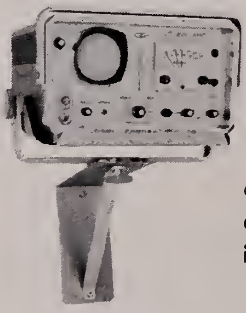

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Carbon Monoxide Intoxication*

Carbon monoxide is a colorless, odorless, nonirritating gas produced under conditions of incomplete combustion. Its danger as an acute intoxicant is well known; above half of the fatal poisonings in the U. S. are attributable to carbon monoxide. Less well known, however, is the ability of carbon monoxide to cause chronic poisoning through long-term exposure. As such it presents a serious public health hazard.

The most common source of carbon monoxide is motor-vehicle exhaust. The average motor vehicle produces exhaust which contains 3.5% carbon monoxide and 11.5% carbon dioxide. The ratio of CO to CO_2 is about 1:2 when the engine is idling, but decreases to 1:10 at cruising speed. As a crude approximation, exhaust gases are diluted about 1000-fold in the air adjacent to heavy traffic. In the absence of air movement, one would expect a fluctuation of the concentration of atmospheric carbon monoxide with the amount of motor-vehicle emission. The city of Los Angeles has a well known problem in regard to air pollution because of its peculiar geographic situation and the nature of the dominant air currents, in addition to its large number of motor vehicles. It is estimated that in Los Angeles motor vehicles emit 9000 tons of carbon monoxide per day, or about 20 tons per square mile.

Pathophysiology

The principal mode of action of carbon monoxide in the body is via a reversible combination with, and inactivation of, circulating hemoglobin, as represented by the equation $CO + HbO_2 \rightleftharpoons HbCO + O_2$. This was postulated as early as 1857 by Claude Bernard, who first suggested that carbon monoxide caused death from anoxia by preventing hemoglobin from carrying oxygen. At that time and for some years later it was believed that carbon monoxide had other specific effects upon various tissues and organs of the body. In 1895 Haldane exposed a mouse to a mixture of oxygen at 2 Atmospheres pressure and carbon monoxide at 1 Atmosphere pressure. Under such conditions it would be expected that most of the animal's hemoglobin would be in the form of carboxyhemoglobin; yet the animal re-

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*Medical Grand Rounds, Mt. Sinai Hospital, May 11, 1965.

Continued

mained conscious and apparently normal. It was felt that compensation took place through a tenfold increase in the amount of oxygen carried in physical solution. Since the animal relied mainly on the physically dissolved oxygen, Haldane had demonstrated that carbon monoxide itself was not toxic but produced its lethal effects by blocking hemoglobin and causing anoxia. Although subsequent investigators have shown that the action of carbon monoxide in the body is not quite so simple, Haldane's experiments led to a philosophy of treating cases of severe carbon monoxide poisoning.

Absorption

In healthy young persons with relatively high-exposure levels, 30-50% of inhaled carbon monoxide is absorbed into the body. The rate of absorption is dependent on a number of factors: (1) the surface area of the gas-exchanging membranes of the pulmonary alveoli; (2) the rate of alveolar ventilation; (3) the rate of blood flow through the lung; and (4) the time required for blood to reach equilibrium with the carbon monoxide.

Affinity for Hemoglobin

The affinity of carbon monoxide for hemoglobin is 200-250 times that of oxygen. This in itself renders hemoglobin relatively unavailable for oxygen transport. In addition, however, the presence of carboxyhemoglobin produces an alteration in the oxygen dissociation curve of the uncomplexed hemoglobin, shifting it to the left so that there is a change in shape from a sigmoid curve to a hyperbola (Figure 1). Thus, except for extremely low oxygen tensions, the oxygen tension in the tissues will have to be lower for oxygen to be released from hemoglobin, and less will be released for a given fall in oxygen tension. This is known as the "Haldane Effect."

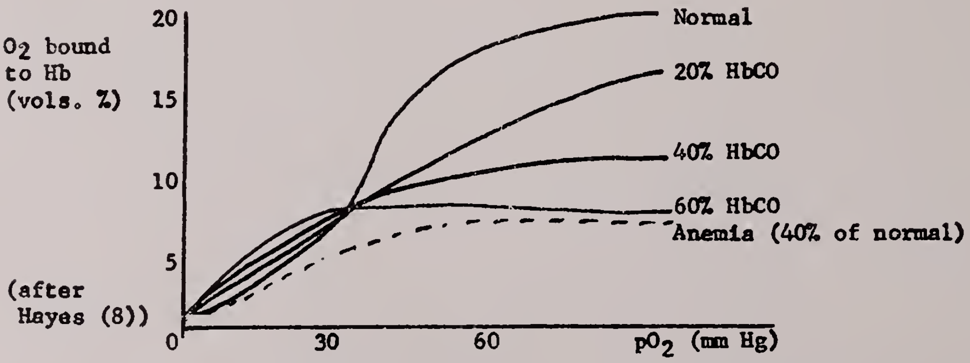

Fig. 1.

Excretion of Carbon Monoxide

Carbon monoxide is excreted predominantly via the lungs. Excretion depends upon alveolar ventilation and the oxygen tension in the inspired gases. In a resting subject breathing room air, the T½ of carbon monoxide elimination is 3-4 hours. Greater activity implies more rapid ventilation and circulation and, therefore, faster excretion. T½ may also be shortened through the substitution of pure oxygen or oxygen under increased pressure.

Since the body has a substantial reserve oxygen-carrying capacity, a small amount of carboxyhemoglobin is of little importance to healthy persons, but in anemic persons, or persons whose blood supply to the various organs is barely adequate, a small decrease in oxygen-carrying capacity may cause serious consequences. The equilibrium relationship between exposure and hemoglobin inactivation is such that 100 p.p.m. are associated with approximately 16% hemoglobin inactivation.

It has been known for many years that the body normally produces a small amount of endogenous carbon monoxide. This phenomenon was first clarified by Sjostrand[18] following the observation that persons with no known exposure to carbon monoxide contained small amounts of carboxyhemoglobin and expired small amounts of carbon monoxide. Sjostrand found that the carbon monoxide was produced during the breakdown of hemoglobin whether this occurred physiologically or pathologically. Engstedt[4] later described in quantitative terms the endogenous formation of CO in hemolytic disease. He found that roughly 0.5% of carboxyhemoglobin could be expected in normal persons and that in hemolytic anemia some subjects had values as high as 2%.

Affect on Eyes

The possibility that carbon monoxide can affect systems other than the hemoglobin system has long been the subject of speculation. Halperin's important study[7] demonstrated that carbon monoxide increases the visual threshold, which means an impairment of visual acuity under conditions of minimal illumination. He found that when oxygen was administered to his subjects and the carboxyhemoglobin level fell, visual thresholds temporarily improved, but that when oxygen was discontinued and room air substituted, the threshold returned to an intermediately impaired value, even though blood carbon monoxide levels did not increase. This suggested that some enzyme or other visual constituent was combining competitively with carbon monoxide and oxygen in the central nervous system or peripheral visual system. Cytochrome oxidase was considered, but rejected because of the fact that even in the absence of oxygen the pressure of carbon monoxide required to halfway saturate cytochrome oxidase is 20 times greater than that required to halfway saturate hemoglobin.

Effect on Muscles

Myoglobin or some similar substance appears to be the prime suspect now, although the affinity of carbon monoxide for this is also less than that for hemoglobin. Nonetheless, the combination of carbon monoxide with myoglobin in the muscles of the body is still postulated to account for much of the extreme muscle weakness which is such a prominent feature of carbon monoxide intoxication. In general, it is felt that it is possible for carbon monoxide to combine with any iron containing pigment, though only the importance of the combination with hemoglobin is well established.

Clinical Considerations

It is fairly certain that simple anoxemia plays the major role in the production of both the pathological lesions and the clinical symptoms of carbon-monoxide intoxication. Physical signs vary with blood levels, but exact correlation cannot be made due to varying states of health or

Continued

fatigue in the individual. Minimal toxicity to carbon monoxide starts at levels in the range of 20% with vague symptoms such as frontal headache, generalized weakness, fatigue, lassitude and drowsiness. These symptoms become progressively more severe when the concentration of carbon monoxide increases beyond 25%, and under these circumstances it is reasonably certain that the symptoms which develop are attributable to carbon monoxide. These may consist of vertigo, nausea, and vomiting.

Toxic Level for Carbon Monoxide

Alterations in physiologic functions are usually not found at levels of carboxyhemoglobin below 20%. Resting pulse, cardiac output and blood pressure are relatively unaffected until levels reach 30%. By 40-50% tachycardia and tachypnea are generally present, and coma ensues, with or without convulsions, at levels of 60-70%. It is generally agreed that a carbon monoxide level of 70% is incompatible with life.

Effect on Brain

It has been demonstrated that the higher centers in the brain are more sensitive to a decrease in blood-oxygen level than are other body tissues, including the lower centers in the brain. Therefore, psychomotor skills would be expected to be affected relatively sooner than others. Schulte[17] found a statistically significant correlation between low levels of carboxyhemoglobin and impairment of psychomotor function, but no correlation with physiologic function. Von Post-Lingen[21] demonstrated an increased threshold of flicker-fusion with carboxyhemoglobin levels below 25%.

Following carbon monoxide hypoxia there is a tendency for cerebral swelling to occur. This causes an increase in the oxygen pressure gradient between capillary and cells, thus producing a secondary hypoxia, which is caused by tissue factors and is independent of the oxygen transport function of the blood. This secondary hypoxia causes the post-anoxic headache which is characteristic after carbon monoxide poisoning, but which is not a part of the symptomatology of carbon monoxide hypoxia itself. Sluijter[19] has found that clinical improvement in cerebral manifestations of carbon monoxide poisoning is closely correlated with improvement in the electroencephalogram. The most characteristic sign is increased voltage of the alpha waves during treatment of patients who are conscious but complaining of severe headache.

Effect on Heart

Electrocardiographic changes in carbon monoxide intoxication are again related to anoxia. Disturbances of rhythm, disturbances of conduction, and ST segment changes may all be present. The specialized conducting system has been said to be the most vulnerable cardiac tissue.

Cosby and Bergeron[1] showed that in dogs the acute and chronic changes were somewhat different. In their acute experiments, T wave and ST segment changes appeared at carbon monoxide levels of 40%, with heart block occurring only with levels above 75%. Necrosis in the myocardium was the characteristic pathological finding. In the chronic experiments, T-wave changes occurred after a week's exposure at 20% concentration, and degeneration of myocardial fibers was the common finding.

In humans it is found that the height of the T wave begins increasing at around 15%. Slight depression of the ST segment ensues at around

35%, and the T waves become diphasic, then inverted, in the 45-60% range.

Chronic Exposure

The whole question of the existence of a chronic state of carbon monoxide intoxication has been subject to much dispute. Katz[9] feels that chronic intoxication constitutes a distinct clinical entity, and he has set down certain criteria for making this diagnosis. These are as follows: (1) blood carbon monoxide of 10% or more; (2) one or more of the following symptoms: headache, dyspepsia, weakness or dizziness; (3) clearing of symptoms 4-7 days after removal from exposure, with daily inhalations of carbogen (95% 0_2 + 5% CO_2); (4) no other medication necessary; (5) freedom from symptoms following reduction of the blood level of carboxyhemoglobin to less than 10%.

Killick,[10] investigating the question of tolerance, has shown that if you expose a person to identical levels and durations of carbon monoxide on several consecutive days, the amount of carboxyhemoglobin resulting from later exposures will be only a fraction of that resulting from the first exposure. Studies of red blood-cell uptake and equilibrium constants in vitro have shown no alterations in these processes. Therefore Killick has felt that either there are changes in the diffusion of carbon monoxide into the blood, or else some metabolic destruction of carbon monoxide occurs. Morgan,[15] on the other hand, is convinced that a compensatory polycythemia takes place. The problem has not yet been resolved.

Treatment

The philosophy of treatment of acute carbon monoxide poisoning has evolved mainly from Haldane's classical mouse experiments. By allowing a patient to breathe oxygen at hyperbaric pressures (usually 2 Atm.), not only may sufficient oxygen be dissolved in the plasma to correct the anoxia rapidly, but also the dynamics of the reaction $CO + Hb0_2 \rightleftharpoons HbCO + O_2$ will be altered so as to give an increased yield of hemoglobin freed from carbon monoxide. This in turn will cause a movement of the oxyhemoglobin dissociation curve of arterial blood back to the right. Secondary hypoxia is also opposed to some degree by the application of high pressure oxygen. Thus in severe cases there is some rationale for giving high-pressure oxygen despite the fact that some of the damage is irreversible.[19]

Oxygen Under Hyperbaric Pressure

Although oxygen under high pressure is generally considered the treatment of choice in severe carbon monoxide poisoning, there is the obvious limitation that relatively few medical centers have hyperbaric chambers, and these are expensive to use. Consequently, alternative approaches have been suggested. Since 1920 much has been written about carbogen (95% O_2 + 5% CO_2) as an effective treatment.[3] The philosophy here is that a small amount of carbon dioxide acts as a mild respiratory stimulant, and thus the blood will be cleared of carbon monoxide faster than with oxygen alone. The method has been condemned by some on the ground that a patient with respiratory depression is already suffering from the effects of an excess of carbon dioxide in his tissues. Nonetheless, the method is still in use and is generally considered beneficial.

Continued

Mercury Vapor Light

Haldane was the first to observe that strong light could be used to accelerate the dissociation of carboxyhemoglobin. The optimal wave lengths for this are 400-430 mμ and 540-570 mμ, and these wave lengths can be obtained using a mercury vapor lamp. Dog experiments have shown that a pump oxygenator along with a facility for exposing the blood to a mercury-vapor lamp can be an extremely effective method for clearing the blood of carbon monoxide.[12] Hypothermia may be used in conjunction to reduce the tissue requirements for oxygen.

Succinic Acid

Although the treatment of acute poisoning by general supportive measures has long been followed, little work has been done on methods of returning the patient quickly to the conscious state. Succinic acid, a powerful respiratory stimulant, has been shown to have beneficial effects in the treatment of coma induced by barbiturates, morphine, insulin, and alcohol, provided failure of the respiratory center has not occurred. Gershon[5] also found it to be of value in shortening the time for return of reflexes in severe carbon monoxide poisoning. Besides its ventilatory effect, succinic acid tends to favor oxyhemoglobin over carboxyhemoglobin in the presence of both carbon monoxide and oxygen in alveolar air and has a direct stimulatory effect on cellular metabolism, particularly in the central nervous system and the functional tissues of the heart.

Sequelae

The question of sequelae resulting from carbon monoxide intoxication has been reviewed by Pfrender.[15] Most investigators agree that sequelae are due to oxygen lack during the acute episode and are related to the length of the period of unconsciousness. It is estimated that permanent sequelae occur in 0.2% of acute poisonings. These usually are neurologic and occur some weeks after the acute episode. Parkinsonism, psychoses, confusion, loss of judgment, amnesia, blindness or partial blindness, and damage to the heart are among the most common sequelae. There is still speculation as to whether these represent specific histotoxic effects of carbon monoxide, as might be suggested by the delay in the onset of symptoms, or whether they fit into the classification of chronic carbon monoxide poisoning, secondary to entrapment of carbon monoxide.

Case Reports

Case No. 1

A 36-year-old separated female under psychiatric care was admitted to another hospital on 11/14/63 after being found comatose in a closed garage with her car running. Artificial respiration was administered by the police, and upon admission to the hospital, blood pressure was 96/60, pulse 110 and respirations 12 and shallow. She was not cyanotic, but was lethargic and complained of nausea and vertigo. She vomited once. Nasal oxygen was administered and by the fifth hour of admission she was oriented and able to take fluids. Physical examination the morning after admission was essentially negative except for pale eyegrounds on funduscopic examination. Hemoglobin was 14, red blood cell count 4 million and white blood cell count 12,500 with normal differential.

The patient was transferred to Mount Sinai Hospital that day, still complaining of headache and nausea. Complete neurological examination was done and was normal except for hyperactive deep tendon reflexes. Spinal tap was normal. An electroencephalogram on the third day of admission showed diffuse low voltage with some increase in voltage following hyperventilation. By the third week of hospitalization the electroencephalogram had virtually returned to normal.

Approximately one week after admission the patient began complaining of a "curtain" in front of her eyes, but ophthalmologic consult revealed no objective evidence of eye difficulty. By the time of discharge, 12/5/63, she was relatively asymptomatic.

Case No. 2

A 42-year-old mechanic and automotive instructor was admitted to Mount Sinai Hospital on 3/30/65 because of symptoms of nausea, epigastric distress, dizziness and chronic fatigue of one year's duration. He also complained of a "loss of circulation" in his arms and legs with frequent episodes of numbness and tingling of the hands, relieved by exercise. His gastrointestinal symptoms were usually relieved by Gelusil and Alka Seltzer, although at times, especially at night, relief was unsatisfactory.

The remainder of the history and all physical findings were unremarkable. Laboratory data revealed hemoglobin of 15.3 gm.%, white blood cell count of 7300 with normal differential, urinalysis normal, serology negative, sedimentation rate 24, stool guaiac negative. Twelve-hour gastric analysis showed a volume of 705 ml. with 74° free acid and 83° total acid. Chest X ray and oral cholecystogram were normal. Stomach X rays demonstrated an ulcer of the lesser curvature of the antrum. Because of the history of chronic exposure to motor-vehicle exhaust, a blood carbon monoxide level was drawn which was 15% (normal less than 5%).

During the hospitalization the patient's gastrointestinal symptoms cleared rapidly on an ulcer regime. He was advised to avoid motor-vehicle exhaust as much as possible.

Arthur Bearon
Mount Sinai Hospital

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7-21 May be secured from Grand Rounds Editor.

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Sufficient for corns was a poultice of berries and cow fat.

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*Bryan, Cyril: The Papyrus Ebers, D. Appleton and Company, New York, 1931, p. 62.

The courage we desire is not the courage to die decently, but to live manfully.

— Carlyle

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ROBERT A. GREEN, M.D.
St. Louis Park, Minnesota

MECHANICALLY INDUCED hemolysis of red cells related to cardiac bypass and prosthetic repairs in the heart is a relatively new problem in clinical hematology. New syndromes are being seen in which it appears that hemolysis results from mechanical trauma to red cells as a direct consequence of the surgery. Hemoglobinemia and hemoglobinuria occur routinely following extracorporeal circulation,* and although they are for the most part transient, there is sufficient injury to red cells not immediately destroyed during the pump run to shorten their life span appreciably. Accelerated red cell destruction in these circumstances may not result in anemia, however, because increased marrow function may compensate for it.

Early Studies

Experimental studies to evaluate the role of mechanical factors in hemolytic anemia following open heart surgical procedures were reported in 1956 by Stohlman et al.,[1] who showed that inserting a lucite prosthesis with the Hufnagel ball valve in the left ventricle of dogs would produce hemolytic anemia. They considered the cause to be mechanical injury to the red cells from impact of the ball against the valve housing. Rose[2] noted postoperative anemia in patients with Hufnagel ball valves placed in the thoracic aorta for the treatment of aortic insufficiency.

The anemia of the post-perfusion syndrome, described by Kreel[3] in 1960, was thought to be due to trauma to red cells, but it was transient and not severe. Prolonged cases of hemolytic anemia of apparently mechanical origin, however, have been reported during the past few years following open heart surgery. The more severe and prolonged cases have occurred mainly in patients who have had Teflon patch repairs of septal defects and in patients who have had aortic valve replacement.

Continued

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*See Test Your Word Score Page 1491.

Causes of Mechanical Hemolysis

The cause of mechanical hemolysis in pumps and tubes, or under other experimental conditions, is not completely understood. Cell lysis may occur because of currents and turbulence and because of other physical influences, such as shear stress, pressure differences, interfacial tensions. In clinical cases, factors of turbulence seem to play the major role, although in some of the Teflon patch cases, hemolysis may be due to impact of red cells on exposed areas of the Teflon patch. In other cases where the Teflon has been completely endothelialized, the problem appears to result from jet stream turbulence through defects in the valve-septal attachment.

Hemolytic Anemia Following Repair of Septal Defects

The first case of severe hemolytic anemia occurring as a complication of open heart surgery in humans was reported in 1961 by Sayed et al.[4] in a patient who had undergone Teflon felt patch repair of an ostium primum defect. Seven cases with similar features have now been reported.[4-7] Morphologic abnormalities of the red cells (fragmentocytes, burrs, helmet cells) and evidence that the hemolysis is intravascular have suggested that it is mechanical in origin and related in some way to the operation. There has been no evidence in these cases that the anemia is autoimmune, and it does not respond to corticosteroids. Two patients have undergone spontaneous partial remission, and five cases have been reoperated. At reoperation, regurgitant jets of blood striking the Teflon patch have been found coming either through cleft aortic cusps of the mitral valve, or through openings where the patch had torn loose from its moorings. Hemolysis in these is considered to be due to impact of the red cells on the patch or to turbulence alone. Two patients recovered fully after reoperation, one of them after covering a bare area of Teflon on the patch with atrial endocardium, the other after anchoring the part of the Teflon patch which had pulled away from the mitral valve attachment. Three other reoperated patients died.

Hemolytic Anemia Following Aortic Valve Replacement

Hemolytic anemia due to mechanical factors alone has also been reported following other types of open heart surgery, notably in cases of aortic valve replacement, when for one reason or another aortic insufficiency persists after operation. In these cases antiglobulin tests are negative; the anemia does not respond to corticosteroids and improves only after the mechanical defect is corrected at reoperation.

Autoimmune Phenomena

Pirofsky[8] has recently described another group of cases of hemolytic anemia following aortic valve replacement which differs from the above in terms of clinical course, serologic tests, and responsiveness to corticosteroids. The clinical course and serologic tests in these cases suggest that autoimmune phenomena are responsible rather than purely mechanical factors. Characteristically, anemia appears fairly early in the postoperative course and is variable in duration and severity, but does not result in death. In four of seven cases, the febrile-lymphocyte-splenomegaly syndrome was also present. Erythrocyte morphology in these cases was not described, although in a personal communication the author stated that he did not feel that at this time the absence or presence of fragmented cells should be used as a differential point between the mechanical and antibody form of hemolytic phenomena.

In contrast to the cases thought to be due to mechanical factors alone, antiglobulin tests were positive in six of seven of these cases, although the reactivity was said to be weak. Because of this and the variability of commercial antiglobulin sera, it is suggested that a battery of tests be performed to detect the positive serologic reaction. These cases also differ in their response to corticosteroids. In four cases in which it was used, prednisone was helpful in correcting the hemolysis.

How and why an autoimmune state develops following aortic valve replacement remains a matter of speculation. It seems unlikely that it is due to infusion of foreign lymphocytes from the large amounts of blood used during surgery, since it does not occur in other types of open heart surgery. The authors speculate that mechanical injury of red cells by turbulence may alter red cell-surface antigens in such a way that they then induce formation of auto-antibodies which are responsible for hemolysis.

Hemolytic Anemia in Valvular Heart Disease Unrelated to Surgery

If turbulence resulting from aortic valve prostheses can produce sufficient injury to red cells to shorten life span and cause hemolytic anemia, one might expect to find this in some cases of rheumatic valvular disease unrelated to surgery. One such case with morphologic changes suggesting red-cell trauma as the causative factor has been discussed by Dameshek.[9] In a study of rheumatic valvular disease by Brodeur et al.,[10] 15 of 21 cases were found to have significantly shortened red-cell survival, although none were significantly anemic. Aortic lesions were considered to be principally responsible for the turbulence resulting in red-cell injury. It seems quite possible that further search may turn up additional cases with significant anemia.

Summary

Hemolytic anemia due to injury of red cells following open heart surgical procedures is a relatively recent development in clinical hematology. Cases have been described in which mechanical factors alone appear to be responsible for hemolysis in some; whereas in others, an autoimmune state is said to be produced, the pathogenesis of which is not clear.

The former frequently require reoperation for correction of a mechanical abnormality producing undue turbulence of blood flow. They are serologically normal and do not respond to corticosteroids.

The latter do not require reoperation, show positive antiglobulin tests, and tend to respond to corticosteroids.

Additional cases of hemolytic anemia due to red-cell trauma are likely to be found among cases of rheumatic valvular disease, primarily with aortic lesions, unrelated to surgery.

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9. Dameshek, W., and Roth, S. I.: Hemolytic Anemia and Valvular Heart Disease: Case Records of the Massachusetts General Hospital. New Engl J Med 17:898, 1964.
10. Brodeur, M. T. H., Sutherland, D. W., Koler, R. D., Kimsey, J. A., and Griswold, H. E.: Red Cell Survival in Patients with Aortic Valvular Disease and Ball-Valve Prostheses. Suppl No III to Circulation 29 & 30:55, 1964.

Free to All Doctors

A supply of leaflets "The Ten Commandments for the Prevention of Alcoholic Addiction" is available to all doctors upon request.* Write: William B. Terhune, M.D.; Silver Hill Foundation, 653 Park Avenue, New York, New York.

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*See Minnesota Med 48:816, 1965.

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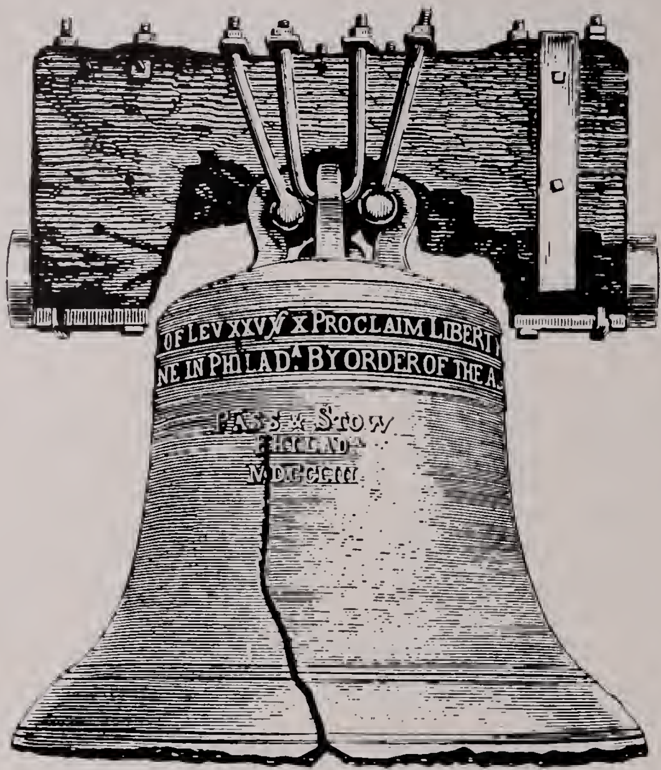
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Abstracts, Briefs and Commentaries

MAMMOGRAPHY NOT INFALLIBLE

Mammography is not, as yet, a screening technique. It is not a simple nor inexpensive procedure. It will not be done by every radiologist. It does not replace biopsy of suspicious lesions.

Selected radiologists (after an instruction course by Dr. Egan) were able to correctly diagnose malignancy in 79% of 475 proven malignancies of the breast. As of now, it is probably agreed that some assistance from mammography may be seen in the following conditions:

1. Women who are difficult to examine because of large breasts
2. Deep-seated lesions
3. Indeterminate lesions
4. Study of the second breast when one breast has been removed for cancer.

Extracts from: Murray M. Copeland, M.D., F.A.C.S.
and Arthur J. Present, M.D.
The American College of Radiology

INCOMPATIBILITY OF INTRAVENOUS SOLUTIONS

For a thesis, Misgen* has studied some of the visible signs of incompatibilities of 34 commonly used intravenous drugs. A thorough pharmacologic testing of all possible drug combinations would be of astronomical proportions if more than two drugs were included in each combination. If one were to test 100 drugs and crossmatch three at a time, a total of approximately 162,000 combinations would be possible.

Misgen has provided a table starring the incompatibility as indicated by particulate matter observed in the solutions when they were crossmatched. This table should be of value to pharmacists or anyone who mixes various intravenous solutions.

It would be well for all doctors when giving mixed intravenous solutions to observe the solution for particulate matter before administration.

Carl O. Rice, M.D.

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*Misgen, Richard: Compatibilities and Incompatibilities of Some Intravenous Solution Admixtures. Amer J Hosp Pharmacy 22:93, 1965. Mr. Misgen is director of Pharmacy, Northwestern Hospital, Minneapolis.

PROTEIN LOSS IN MALIGNANCY

Malignant lesions of the gastrointestinal tract are commonly associated with hypoproteinemia. Sixteen patients with carcinoma of the gastrointestinal tract and three with carcinoma elsewhere were studied. The protein loss into the gastrointestinal tract and albumin degeneration rate were measured in a series of patients with I^{131}-labeled albumin. Excessive loss of protein into the intestine was demonstrated in two cases of carcinoma of the stomach, one of the esophagus, and one of the colon. In one patient resection of the colon lesion resulted in a remarkable reduction in protein loss. It is suggested that the major source of protein loss is the tumor itself and adjacent mucosa.

Courtesy of References and Reviews
Journal of the American Medical Association

Sum, P., Hoffman, M., Webster, D. R.: Canad J Surg 7:1, 1964

GASTROINTESTINAL BLEEDING OF "UNKNOWN ORIGIN"

Gastrointestinal hemorrhage in the pediatric age group, particularly that of rectal issue, is studied by comparison of three case series, including 48 cases of bleeding Meckel's Diverticulum, 16 cases of peptic ulcer, and 79 cases of bleeding due to "unknown cause." The mathematical probability of finding a Meckel's Diverticulum at laparotomy for rectal bleeding is calculated for this series, and the rate of diagnostic accuracy is found to be less than 66%. The probabilities of origin of hemorrhage in the "unknown bleeder" are discussed. The conclusion is reached that larger numbers of such cases than heretofore realized are probably because of acute peptic ulceration of the stomach or of the duodenum. Certain clinical recommendations are made based upon this hypothesis.

Courtesy of References and Reviews
Journal of the American Medical Association

Brayton, D.: Amer J Dis Child 107:287, 1964

CONTROLLED TRIAL OF PROPHYLACTIC PORTACAVAL SHUNT SURGERY

The Boston Inter-Hospital Liver Group has conducted a controlled hospital trial of prophylactic portacaval shunt surgery in patients with cirrhosis and esophageal varices. The first 50 patients are reported. There were nine deaths among 28 patients who were operated on, and eight deaths in the 22 controls. Five massive hemorrhages occurred among the controls, three of which were fatal, and two massive hemorrhages, probably from duodenal ulcer, in the surgical group. Varices have persisted unchanged in only two of the 19 survivors in the group operated on, and in 11 of the 14 survivors in the control group. Hepatic precoma is a continuing problem in four of the surgical and in one of the control patients. The over-all survival is greatly improved in patients who were selected for this study when compared with the whole population with esophageal varices, but within the study no significant difference is yet apparent between the surgical and control patients. A longer follow-up and a larger number of patients are needed.

Courtesy of References and Reviews
Journal of the American Medical Association

Garceau, A. J.: New Engl J Med 270:496, 1964

ULTRA SOUND

An *International Conference on Diagnostic Ultrasound* was held at the Pittsburgh Hilton Hotel on May 20-22, 1965. The conference was well attended by overseas representatives with the exception of Russia.

The use of diagnostic ultrasound in medicine has now reached a stage of acceptance by our profession to encourage production of commercial medical instruments.

Clinical papers reporting the use of ultrasound in locating and removing foreign bodies in the eye, measurement of the size of the eye and the diagnosis of intraocular and extraocular pathology were given.

The diagnostic value of displacement of the mid-line echo by space-occupying lesions and measurement of the lateral ventricles of the brain were described. The use of ultrasound for the measurement of the mitral valve and for the study of other functional cardiac pathology was reported.

Papers on the diagnostic value of ultrasound in the study of abdominal organs such as the liver and spleen were not too encouraging with present techniques. A special paper on the toxicity of ultrasound at diagnostic power levels revealed absolutely no trace of harm. This was a monumental and exhaustive study supported by Smith Kline Instrument Company.

Considerable advances were reported in the use of ultrasound in studying the contents of the female abdomen in gynecological and obstetric conditions. Scottish and Australian work was the most outstanding. The contents of the pregnant and nonpregnant uterus in the later stages of uterine enlargement were easy to differentiate. Hydatidiform mole was clearly seen as a "snow-storm" in the uterus as opposed to fetal parts. The early pregnant uterus could be seen through a full bladder. A number of commercially available instruments used in most of the clinical studies were introduced.

At the workshop conference at the end of the meeting future needs and further development were vigorously discussed.

J. J. Wild, M.D.
Minneapolis, Minnesota

NICOTINIC ACID IN HYPERCHOLESTEREMIA

Forty-one patients with hypercholesteremia and peripheral or coronary arteriosclerosis were treated with 1.5-7.0 gm of nicotinic acid daily for 6 years. Rapid reduction of cholesterol and all lipid fractions was achieved in all patients without change in diet. Three deaths from arteriosclerotic heart disease occurred shortly after onset of therapy, but none thereafter. While on therapy all patients had normal lipid levels. Acanthosis nigricans was seen in four patients and disappeared promptly on discontinuation of therapy. Diabetes mellitus was temporarily aggravated in three of five patients. This medication seems singularly well-suited for a wide range study on the influence of reduction of cholesterol levels on life expectancy.

Courtesy of References and Reviews
Journal of the American Medical Association

Mahl, M., and Lange, K.: Amer J Med Sci 246:673, 1963

TRUNCAL SHOTGUN WOUNDS

These are characteristically civilian or "peace time" wounds, but many resemble war injuries, with extensive tissue loss or destruction and multiple injuries. The broad shot pattern frequently leads to thoracico-abdominal injury and often results in multiple organ and also multiple system injury with involvement of cardiovascular, respiratory, gastrointestinal, and neurologic systems. These wounds are usually associated with extremely high morbidity and mortality rates. The weapon is frequently chosen by those making a sincere attempt at suicide. Sporting shotgun accidents are commonplace.

Hospital records of 1,487 patients were reviewed. One hundred fifty-four wounds were inflicted with shotguns. One hundred and three of these involved the trunk and serve as the basis of this report. Sixty-seven per cent of such wounds were in Negroes. One hundred and three who sustained shotgun injuries survived long enough to reach the hospital. Eighty-one patients with truncal wounds survived, while 22 died, a survival rate of 79 per cent. A 12-gauge weapon with No. 6 shot was most popular. Five patients had self-inflicted wounds as a suicide attempt. The severity of this type of injury lessens as the distance between the gun and the patient increases, due to scattering of the pellets.

Patients were placed into four groups according to the type of therapy employed:

Group I

Patients in this group were less severely injured; their wounds with tetanus prophylaxis were treated locally together with observation during course of recovery. There were 12 patients with 100 per cent recovery in this group.

Group II

These were more severely injured persons who did not require major surgery. There were 11 patients with 100 per cent recovery; one patient required bilateral tube thoracostomy for bilateral hemopneumothorax.

Group III

Nineteen patients underwent a major procedure requiring general anesthesia but not involving the pleural or peritoneal cavities. These procedures generally required immediate debridement of wounds plus exploration of major vessels in the neck or groin. Three patients required tube thoracostomy; ten required blood transfusions. There were 16 survivors and three deaths. The survivors received an average of 1500 cc. of blood, and those who expired an average of 4000 cc. Eight major complications developed in six patients. Twelve secondary operations were performed on eight patients.

Group IV

This group of 61 patients included those who required abdominal, thoracic, or thoracico-abdominal operations. There were 42 survivors and 19 deaths. Thirty-two injuries were confined to the abdomen, 25 were thoracico-abdominal, while three were thoracic only. Sixteen patients undergoing laparotomy required tube thoracostomy also. The colon and small intestine were involved in 32 patients. The liver, stomach, and kidney were involved in 19, 15, and 14 cases, respectively. Injury to the diaphragm occurred in 13 cases and to the spleen in 10 cases. In most cases more than one organ, sometimes several, were involved.

Survivors in this group received an average of 2750 cc. of blood, while those who did not survive received an average of 4500 cc. Twenty-eight patients had a major body-wall defect requiring some type of reconstructive procedure to close; sixteen of these defects were in the chest wall and 12 in the abdominal wall. Forty-one major complications developed in 28 patients. Four patients had evisceration when admitted. There occurred six fecal fistulas in four patients, two of whom expired. Two patients developed massive upper gastrointestinal hemorrhage and both died. One patient with biliary fistula following extensive liver damage survived with spontaneous closure of the fistula. There were seven pulmonary complications. One patient died from pneumonia, and one with infection of the abdominal wall with gas-forming organisms following a colon resection. Postoperative complications were considered the cause of death in 10 of 22 patients who expired. Secondary plastic operations were frequent. Two arteriovenous fistulae were excised.

Shotgun wounds are a distinct injury, different from other penetrating wounds or those caused by other types of firearms. Multiple organ and multiple system injuries are common. Thoracico-abdominal wounds are frequent. Body-wall defects demand reconstructive closure. Complications are common and frequently the cause of death. Secondary surgery is often required. Successful management demands rapid institution of effective resuscitative measures and a broad surgical knowledge.

Stanley R. Maxeiner, Sr., M.D.
Minneapolis, Minnesota

Fitzgerald, John B., Quast, Don C., Beal, Arthur C., Jr., and DeBakey, Michael E.: Surgical Experience with 103 Truncal Shotgun Wounds. J Trauma, January 1965

ANESTHESIA IN HEAD INJURIES

Proper anesthetic management of patients with head injuries and associated trauma requires that a philosophy of total patient care be practiced. Repeated evaluation of physical, hemodynamic, and neurological status is required. The presence of shock in patients with head injuries usually indicates associated, more serious injuries which must be sought and treated or excluded. Anesthetic management and priority of treatment of multiple injuries are enumerated. General anesthesia is usually preferred and has not increased the severity of neurological impairment due to trauma.

Courtesy of References and Reviews
Journal of the American Medical Association

Beck, G., and Neill, L.: Anesth Analg 42:687, 1963

TONSILLECTOMY DEATHS

Ninety three deaths due to tonsillectomy reported in a five-year period are analyzed. Postoperative hemorrhage occurred in 62 cases. Errors of anesthesia accounted for the majority of the remaining 31 deaths. The traditional management of these cases is criticized and suggestions are

Continued

made to reduce the 1:10,000 mortality. The difficulty in reanesthetizing bleeding patients is stressed.

Courtesy of References and Reviews
Journal of the American Medical Association

Tate, N.: Lancet 2:1090, 1963

PANCREATIC BIOPSY

Of 159 patients undergoing pancreatic biopsy, the complication rate was 9.5% and the mortality rate was 3.8%. There were three deaths in 25 Silverman-needle biopsies and two deaths in 130 wedge biopsies. The chief complication from this procedure is pancreatitis. Pancreatitis following a needle biopsy is due to the needle's entering a part of the duct system and the consequent escape of pancreatic juice into the substance of the pancreas. Thus, pancreatitis can develop without a fistula. This has been true even with transduodenal needle biopsies. Because of its risk, pancreatic biopsy should not be performed indiscriminately. It should not be done for unresectable lesions nor should it be used for resectable lesions which clinically appear to be carcinoma. Biopsy of the pancreas should be reserved for those resectable lesions which do not have the obvious clinical features of neoplasm.

Courtesy of References and Reviews
Journal of the American Medical Association

Schultz, N. J., and Sanders, R. J.: Ann Surg 158:1053, 1963

SIGMOID VOLVULUS

On the basis of this review and experience, a plan for treatment of sigmoid volvulus was established: 1) immediate operation for acute, fulminating type; 2) nonoperative decompression of the volvulus with proctoscope and rectal tube for subacute, chronic type, followed by elective resection in seven to ten days in most instances. In the series reported, where gangrenous bowel was suspected, where proctoscopic decompression was unsuccessful, or where at proctoscopy the mucosa appears friable, discolored, or bloody, laparotomy was indicated. If the bowel was viable at surgery, operative detorsion was done with a rectal tube threaded past the twist and sutured in place at the anus. If the bowel was gangrenous, then an obstructive resection was done. In those cases successfully reduced, where age or other radical conditions contraindicate elective resection, a low-fiber diet and wetting agents were of benefit.

Courtesy of References and Reviews
Journal of the American Medical Association

Abrams, B. L.: Arch Surg 87:1033, 1963.

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*It is not the challenge of today that drives men mad, but the remorse of yesterday and the dread of tomorrow.**

Theodore S. Raiford, M.D.
Ashville, North Carolina

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*The Three Days of Medicine, N Carolina Med J 26:185, 1965.

O Lord — if there is a Lord; save my soul — if I have a soul. — Renan

Book Reviews

Very few can be trusted with an education. — Louis Imogen Guiney

SURGERY OF FACIAL FRACTURES — **Reed O. Dingman, M.D. and Paul Natvig, M.D. W. B. Saunders Co. Philadelphia, $22.50.**

This volume presents a thorough resume of the modern management of simple and severe facial fractures. Though it is most useful to the plastic and maxillofacial surgeon, basic fundamentals are emphasized, making it a valuable reference work for general surgeons, surgical specialists and dentists treating facial injuries.

Separate chapters dealing with dental occlusion and intermaxillary fixation are detailed and well illustrated. These fundamental aspects of fracture reduction and fixation are adequately emphasized.

The diagnosis of these fractures can often be made on clinical examination, but roentgenographic confirmation is necessary. To satisfactorily visualize these difficult areas diagrams of the various roentgenographic positions are included.

The basic methods of reduction and fixation of facial fractures is thoroughly covered. Open operation at fracture sites with fixation of the bony fragments with stainless steel ligatures is well discussed and illustrated. Also included is a separate chapter on the more difficult problem of facial fractures in children. And last but not least, the authors have prefaced the text with several profiles of pioneers who have laid the foundation for modern care of facial bone injuries.

Lyle V. Kragh, M.D.
Minneapolis, Minnesota

INDUSTRIAL AND TRAUMATIC OPHTHALMOLOGY — **Symposium of the New Orleans Academy of Ophthalmology. C. V. Mosby Co., St. Louis, 1964. 321 pages. Illustrated, references, index. Price $14.50.**

This book will find wide use among industrial physicians, compensation experts and ophthalmologists. Seven experts in this broad field have contributed chapters and a round table discussion on the following subjects: Plant vision safety and screening; emergency eye care; visual requirements of driving; lead trauma involving the eyes; chemical and radiant energy injuries; protective eye wear; disability rating of eye injuries; immediate and delayed pathology of ocular trauma. The subjects are presented in detail. The volume is well edited and illustrated. To my knowledge there is no comparable work available.

William S. McClanahan, M.D.
Minneapolis, Minnesota

BAHAMA INTERNATIONAL CONFERENCE ON BURNS — **Dorrence and Co., 1964**

This conference on burns was conducted by a group of physicians who could speak authoritatively on each of these problems relative to burns.

The monograph deals with the entire problem of burns and includes some well-documented research work.

Clinical application to the treatment of burns has been adequately detailed and illustrated. Treatment of shock and fluid imbalance are also described. A few color illustrations add some charm.

For the plastic surgeon who has some interest in the practical application of his art, this monograph should serve an excellent purpose. To other physicians who are interested in the burn problem, this book should be well worth a few hours of concentrated study.

Carl O. Rice, M.D.
Minneapolis, Minnesota

OUTLINE OF UROLOGY — **C. D. Creely, McGraw Hill Book Co., Toronto, 1964. p. 385.**

This pocket-sized textbook of urology is beautifully bound, well illustrated and succinctly written in the very excellent manner in which the author has conducted his teaching at the University of Minnesota Medical School.

This book should be on the office shelves of every practitioner who may from time to time desire some brief enlightenment in the field of urology. For the medical student who is becoming acquainted with his clinical material, this is an invaluable textbook, concise, well organized and adequately illustrated with line drawings or X-ray films. The references and bibliography at the end of each chapter are sufficient for anyone who wishes to make a more detailed study. The index is well done.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Space contributed as a public service by this magazine.

Don't turn your back

Photo contributed by Paul Duckworth.

Your community needs your experience in helping to maintain its American tradition of people voluntarily helping people. Whether you are an executive with a national corporation, a local business or professional leader, you can help set the example by taking an active role in your United Way programs.

Offer your skills to help in planning for human needs, to assist in budgeting for organizing and conducting United Way campaigns in your community.

Only when goals are met can human needs of those who require care, love and hope be fulfilled, and communities made healthier and happier places for all citizens today and tomorrow. Participating in your United Fund or Community Chest is one way to affirm your confidence in the American way of life.

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25 million families benefit from child care, family service, youth guidance, health programs and services for the armed forces through 34,500 United Way agencies.

Special Article

Family Planning in the City-County Hospital Setting

- A
- Preliminary
- Report

ERICK Y. HAKANSON, M.D.*
St. Paul, Minnesota

ONE OF the necessary responsibilities of an obstetrical department in the maintenance of optimum health for the indigent and disadvantaged patient is to provide help in family planning.

Unfortunately, in the past, contraception has been such a controversial subject that meaningful discussion of it has been limited to the scientific community and has been shunned by politicians and government officials at all levels. This lack of public awareness has led to vast areas of ignorance, misinformation, and apathy. These facts, together with political and religious opposition, have relegated birth control largely to a matter of private initiative. The result has been that those patients who were able to afford private care were able to take advantage of whatever scientific information and/or techniques were available, whereas the indigent patient had nowhere to turn for help. Another direct, but unfortunate, result of our past public health policy in this matter has been to promote higher fertility rates in that segment of the population which least wants and, from many viewpoints, should not have large families.

Attitude of the Public

Fortunately, in the past five years, public attitudes concerning contraception have changed radically, and discussion of every aspect of it has become part of the public dialog. For example, the Gallup Poll on January 6, 1965, reported that 81 per cent of the people interviewed favored making birth control information available anywhere in the United States to anyone who wants it. This was the largest percentage recorded and was largely due to the changing attitudes of the Catholic segment of the population. In June 1963, 53 per cent of Catholics interviewed said they believed birth control information should be available anywhere in the United States. In January 1965, 78 per cent held this view. This does not mean that

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*Head, Department of Obstetrics & Gynecology, Ancker Hospital.

Continued

Catholics approved of all methods of birth control, but only that such help should be available for those who want it.

Religious Barrier

At the present time there is a rather remarkable consensus regarding contraception. For example, the major religious denominations agree:

1. On the objectives of family limitation; 2. On the general need for family limitation; 3. On the right of people to have help toward this end; 4. On the spending of public money for this purpose, with the important provisos that any such programs be voluntary, and that no one be advised to violate his religious convictions.

What controversy remains involves largely questions of methodology, and it is not inconceivable that even this remaining point of controversy can be largely mitigated, or removed entirely, by future developments. As a result of this rather widespread agreement, public health officials and government leaders are finally taking the necessary steps to make family planning services available to the disadvantaged portion of our society. More and more cities and states are setting up programs for this purpose. In Minnesota, public health programs for family planning have not been developed previously because of an 1886 law which classified all contraceptives as obscene materials and therefore illegal.* It is hoped that the present legislature will eliminate this archaic law so that the various state and county agencies can implement programs that have already been proposed.

Contraceptive Methodology

As noted above, there has been a revolutionary change in the contraceptive methodology. There can be no doubt that the discovery of the oral contraceptives has been one of the most important advances in this field. In addition, their use has been responsible, at least in part, for the changing public attitudes noted above. More recently, the perfection of the intrauterine contraceptive devices has added still another dimension in contraceptive technology.

The Ideal

In spite of these advances, the ideal contraceptive is still not at hand. Such contraceptive technique should meet the following criteria:

1. It must be reliable.
2. It must be simple to use.
3. It should be free of undesirable or deleterious side effects.
4. It should be inexpensive.
5. It should be reversible.
6. It should be acceptable to people of all cultures and religious beliefs.
7. It should require minimum motivation.

All of the above criteria are self-indicative except for the factor of reliability. Obviously any technique must have a certain level of effectiveness in order to be acceptable. The exact level of this reliability varies according to individual needs and preferences from being absolute and permanent to only partial and temporary.

Pearl's Formula

The most commonly used measure of effectiveness is still Pearl's formula where

$$R = \frac{\text{Total number of conceptions x 1200}}{\text{Total months of exposure}}$$

This formula is not precise because of a selection factor which tends to make failure rates decline as the period of contraceptive use increases. There have been a number of attempts to overcome this objection, but as yet the application of sophisticated statistical techniques for the comparison of contraceptive practices of the general population has not met with success. It has been calculated that R would have a value of approximately 80 in a so-called normal, uncontrolled exposure for American couples. However, this figure has been estimated to be as high as 120 in certain Central and South American countries. In a perfect contraceptive, R would be 0. Reliability should also be evaluated in terms of its use-effectiveness rather than its theoretical effectiveness. A method may be close to zero in failure rate in the laboratory or when perfectly applied. However, due to

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*This law was revised by unanimous vote of the 1965 session of the Minnesota Legislature.

TABLE 1
Characteristics of Common Birth Control Methods*

Method	Effectiveness	Deleterious Effects		Difficulties of Use			Relative Values Cost
	Preg. per 100 yr.	Side Effects	Long-term	Repeated Action	Repeated Supplies	Professional Hr./100 yr.	
Intrauterine	1-3	+	?	0	0	10-25	1
Oral	1-3	+	?	D	Y	10-25	24
Condom	5-15	0	0	C	Y	0	6
Diaphragm & Jelly	5-15	0	0	C	Y	10-15	8
Aerosol foam	10-30	0	0	C	Y	0	8
Withdrawal	10-30	0	0	C	0	0	0
Jelly or cream	20-40	0	0	C	Y	0	8
Foam tablet	20-40	0	0	C	Y	0	6
Rhythm	20-40	0	0	C	0	+	0

D—Daily, C—Each coitus, Y—Yes, N—No.
*Adapted from Calderone, M.S.: Manual of Contraceptive Practice, Williams & Wilkins, Baltimore, 1964.

a host of factors, this same technique may have a significant failure rate when used by the population at large.

The Reliability of Methods

Table 1 is a comparison of the various methods in use throughout the world with respect to some of the factors mentioned above. It will be noted that there is just as much variation in reliability with the same method as there is with different methods. This observation emphasizes the fact that the success of any method depends on multiple inter-related factors such as natural fertility, educational status and intelligence, economic level, religious bias, and many other cultural influences. In more concrete terms, it should be fairly obvious that while a given technique may be eminently satisfactory in the high income, high education Crocus Hill district of St. Paul, it may not be successful in the Selby-Dale area.

Table 2 is from the data of Westoff et al.[1] and is based on an analysis of 1,165 couples living in seven of the largest cities and their suburbs who were interviewed in 1957 about six months after the birth of their second child. This table gives us an estimate not only of the choice of methods in general use before the introduction of oral contraceptives, but also of their use-effectiveness. It points out that for all methods combined there was an average failure rate of 22.4 per 100 woman years. We can conclude from this that urban Americans were using birth control techniques quite effectively. Moreover, on re-interview three years later, it was found that those couples who had completed their families had a failure rate of only 3.7 per 100 years for all methods combined. This result points out the other single most important consideration in the application and use-effectiveness of these contraceptive methods — the factor of motivation.

TABLE 2
Months of Use of Contraception, Accidental Pregnancies, and
Failure Rate Per 100 Years of Use, by Method:
USA Metropolitan Areas*

Method	Months of Use		Accidental Pregnancies	Failure Rate
	No.	Per cent		
Condom	10,062	35.2	116	13.8
Diaphragm	5,679	19.9	68	14.4
Withdrawal	1,287	4.5	18	16.8
Rhythm	4,179	14.6	134	38.5
Douche	1,265	4.4	43	40.8
All other**	6,135	21.4	155	30.3
All methods	28,607	100.0	534	22.4

*Adapted from Westoff, C. F. et al.
**Including combined and alternate use.

Continued

Motivated couples can use the more complicated techniques of diaphragm and jelly with almost perfect success. Likewise Tietze[2] has shown that the rhythm method can be made to be reasonably reliable in couples that are sufficiently motivated and under medical supervision.

Any successful approach to family planning for indigent and semi-indigent patients should give a proper emphasis to the above factors. It has been widely assumed that one of the reasons for the higher fertility of the indigent patients has been their lack of motivation. However, the studies of Rainwater[3] have pointed out the relationship of motivation to the total cultural setting of the indigent family. Numerous reports have documented the fact that the low-income, low-education status patient can use the oral contraceptives very successfully. Whatever the merits of the above reason, there is documentation for the following conclusions:[4,5]

1. Lower income families want smaller families on the average than high income families.
2. Nonwhites want smaller families than whites.
3. The overwhelming majority of indigent and semi-indigent desire help in family planning.
4. The less educated tend to use relatively less reliable methods of contraception than the more educated.
5. While the indigent patient may have less motivation than his upper-class counterpart, there is evidence that this lack, at least in part, is due to the conditions under which he has in the past received whatever contraceptive help was available.

Our experience at Ancker, which admittedly is recent and on a rather small scale, tends to corroborate the above observations. For example, 300 consecutive patients who were married and living with their husbands were interviewed on the post-partum ward. Of the total group, only 14 per cent stated that they had been trying to get pregnant. However, of those who had four or more children at home, only 2 per cent had been trying to get pregnant, and most of these gave as their reason the desire of a second husband to have children. Approximately 70 per cent stated that they had been attempting some form of birth control, including rhythm. It was evident, however, that in a majority of the patients contraception was applied either intermittently or haphazardly. It was particularly evident that many of the couples using the rhythm method had not been under medical supervision and were, in fact, using the method in such a manner as to actually hasten a pregnancy. Although almost 90 per cent of the patients stated that they now wanted help to prevent the next pregnancy, most of them had reservations about the methods they had used or heard about in the past. If, however, the time were taken to explain the various methods, most of their objections could be answered to their satisfaction. It came out during these interviews that there were marked individual preferences as to their choice of contraceptive methods.

On the basis of these preliminary inquiries, a more comprehensive program of family planning was started at Ancker Hospital. In addition to offering the oral contraceptives, a rhythm clinic was initiated. Also, one vaginal foam was added; and an intrauterine device is being inserted in carefully selected patients. As soon as funds become available, all reliable methods will be offered, and in cooperation with other agencies, evening clinics may be considered to make them more accessible.

This program has been in operation for less than a year and no data can be reported as yet. The initial response to family planning by the indigent patient has been excellent. It has also become clear that for persistent use of a contraceptive method, good rapport with the patient and sufficient personnel for thorough followup are essential. The acceptance and results of the various methods will be the subject of a subsequent report.

Summary

Family planning has become an accepted function of public health agencies and facilities. Such programs should take into account the diverse personal, religious, and cultural backgrounds of the low-income patient, and

offer a comprehensive program to suit individual needs. Preliminary evidence indicates that such a program could be successfully applied to nearly all patients.

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Paleopathology V*: Peruvian

Examination of Pre-Columbian Peruvian mummies reveals that the early inhabitants of Peru, unlike the ancient Egyptians, were relatively free of two major pathologies: arthridites and arteriosclerosis. Since preservation by embalming was not an early Peruvian practice or ritual, most of the corpses were eviscerated and dried previous to wrapping, thus confining examination to the bone structure.

Tumors, it appears, were numerous — especially hyperostoses cranii, due to an endocranial tumorous condition of the dural membrane. Also prevalent were ivory-like osteomae on mummy skulls and mandibles.

As for oral diseases: whereas caries did not appear to be a problem, pyorrhea due to heavy calculus deposits was very common and doubtless the main cause of the edentia so frequently noted in these mummies.

Infant mortality must have been phenomenally high in ancient Peru, as indicated by an abundance of infant mummies in the Field Museum collection, most of them young children — either full-term or under two years of age. A puzzling question is: why did these infants die? The cause or causes are not apparent on the mummy remains and cannot be determined by roentgenographic examination.

In contrast with an incidence of 40-per-cent morbidity in Egyptian mummies, 53 Peruvian mummies revealed a significantly lower incidence of 10.52 per cent.

Why the striking differences between the ancient Egyptians and the Pre-Columbian Peruvians? Were climate and diet determining factors in the relative frequency or rarity of various diseases? What other influences may have been operative? These are some of the intriguing questions future paleopathologists will doubtless answer.

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*See Minnesota Med 48:908, 48:1020, 48:1250, and 48:1278, 1965.

Derivatively Speaking

Condyloma: from Greek *kondylos,* a fist or joint.

Laugh, and the world laughs with you. Snore, and you sleep alone.

— Author unidentified

The Stethoscope Song

There was a young man in Boston town,
He bought him a stethoscope nice and new,
All mounted and finished and polished down,
With an ivory cap and a stopper too.

It happened a spider within did crawl,
And spun him a web of ample size,
Wherein there chanced one day to fall
A couple of very imprudent flies.

The first was a bottle-fly, big and blue,
The second was smaller, and thin and long;
So there was a concert between the two,
Like an octave flute and a tavern gong.

Now being from Paris but recently,
This fine young man would show his skill;
And so they gave him his hand to try,
A hospital patient extremely ill.

Some said that his *liver* was short of *bile*,
And some that his *heart* was over size,
While some kept arguing, all the while,
He was crammed with *tubercles* up to his eyes.

This fine young man then up stepped he,
And all the doctors made a pause;
Said he, The man must die, you see,
By the fifty-seventh of Louis's laws.

* * *

Then out his stethoscope he took,
And on it placed his curious ear;
Mon Dieu! said he, with a knowing look,
Why, here is a sound that's mighty queer!

The *bourdonnement* is very clear, —
Amphoric buzzing, as I'm alive!
Five doctors took their turn to hear;
Amphoric buzzing, said all the five.

There's *empyema* beyond a doubt;
We'll plunge a trocar in his side.
The diagnosis was made out, —
They tapped the patient; so he died.

* * *

Now use your ears, all you that can,
But don't forget to mind your eyes,
Or you may be cheated, like this young man,
By a couple of silly, abnormal flies.

Oliver Wendell Holmes

Medicine and Religion

The Dimensions of Medicine*

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EVERY DOCTOR likes to think of himself as something of a scientist. The practice of medicine, like scientific research, calls for accurate observation, logical thinking and objective evaluation. In the course of his training, the physician has had some indoctrination in these disciplines. He has been required to master a considerable body of knowledge, the preclinical sciences, before he begins to work with patients.

Most young doctors, when their training is over, are eager to pit their new knowledge and skill against disease in the practice of medicine. A few, however, attracted by the still unexplored reaches of medicine, elect to remain in medical research. The driving curiosity that is an essential for every research scientist may overcome an urge to practice that is based upon the practical rewards of medicine and the opportunities for service that it brings.

The ultimate value of choosing medical research as a career may be greater than choosing medical practice. If the medical scientist is able to accomplish a break-through in some important area, or even to help lay the groundwork for some important discovery, he may become a greater benefactor to humanity than he could ever be as a practicing physician. Not every medical scientist can make the contribution of a Salk or a Fleming, but fortunately, many dedicated medical people continue to elect research careers.

The area of pure research may be looked upon as the scientific dimension of medicine. This devotion to an investigative career in some basic medical science has led to discovery of the antibiotics, the conquest of diabetes and pernicious anemia, the understanding of genetic disease, and the vast benefits of immunization.

While some few elect medical research, a far greater number of young physicians are eager to slay the dragons of disease and move directly into practice. This is the therapeutic dimension of medicine, where emphasis is upon treatment that will lead to healing. With a grounding in the basic sciences of physiology, pathology and pharmacology, the physician mobilizes every resource of knowledge and skill to heal his patients.

Analytical Thinking

When he meets a sick patient, the doctor's mind operates like a computer. The patient's complaint triggers a process of analytical thinking that almost automatically produces in the doctor's mind a list of possibilities, arranged in the order of statistical probability, even before he begins his examination. If the symptom is a pain in the right lower quadrant, appendicitis will probably be at the top of the list; ureteral stone and mittelschmerz will be somewhere in the middle, and ruptured ectopic pregnancy may be near the bottom. Then begins the clinical search, in which careful observation and clinical acumen eliminate one by one all the possibilities except the correct one. If the symptom is a high fever, an entirely different mental check-off list appears, with pneumonia, septicemia and numerous names ending in *itis* suggesting themselves as possibilities. Again,

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*Presented at the 112th Annual Meeting of the Minnesota State Medical Association, May 17, 1965, Minneapolis, Minnesota.

**Director of University of Illinois.

the training, experience and astuteness of the physician will complete the process of elimination and diagnosis.

A physician's scientific training will not allow him to be content with treating the symptom and neglecting its cause. A common drug might relieve the abdominal pain or reduce the temperature, but the cause of the symptom would remain untouched. Only if the symptom can be traced to its origin can the cause of the illness be abolished. Modern medicine will never be satisfied with "symptomatic treatment," until every effort has been made to discover and eliminate the fundamental cause.

Psychosomatic Evaluation

If the chief symptom is emotional rather than physical, the diagnostic process is switched into an entirely different channel. Anxiety or depression shifts the search into the dimension of personality, for these signs indicate that the cause is broader and deeper than merely physical. In the therapeutic dimension, the physician sees a disease that needs treatment. In the dimension of personality, the patient must be seen as a whole person. This involves evaluation of the emotional and intellectual elements of personality — that is, how the patient feels and what he thinks, as well as his physiology — how his body works.

Disturbances of thought and feeling have long been considered the province of the psychiatrist. The regular physician often feels ill at ease in dealing with such disorders and may be inclined to refer his patient. While the psychiatrist is more closely concerned with the dimension of personality in his work, the rise of psychosomatic medicine has made it clear that no physician can avoid involvement in the emotional problems of his patients. He is the first to encounter these emotional problems. His patient may or may not be willing to consult a psychiatrist.

The dimension of personality also calls to mind a diagnostic check-off list, but one less precise than that for physical illness, and the process of elimination is far more complex. Since anxiety, like pain or fever, is only a symptom of deeper psychic conflict, the common causes of such internal discord must be passed in review, ranked according to their frequency.

The experience of the psychiatrist indicates that interpersonal conflicts will be at the top of such a list. The specific persons most often implicated are members of the family, such as parents, siblings or spouse. A second common cause of anxiety is some form of value conflict, in which the person has violated some system of values or moral standard. A third cause of conflict is a faulty personality pattern acquired in the developmental period. Over-aggressiveness and hostility, excessive dependency or pathologic seclusiveness may be causing the patient psychic "pain," impairing his relationships with other persons, and producing alienation.

What makes the dimension of personality more complex is that neurosis is a form of self-deception; hence, the patient usually does not understand his own disorder. The information he offers in the diagnostic search may be useless or even misleading. An important part of the treatment is to help him understand himself better and to reorganize his defective attitudes.

Psychotherapy

The underlying cause of most neurotic and personality disorders will be one of the following: (1) faulty interpersonal attitude, (2) warped attitude toward oneself, (3) value conflict, (4) developmental disorder of personality. Behind each of these is a disturbance in intellectual and emotional attitudes that the patient must be helped to understand and correct. This process of review by doctor and patient is called psychotherapy.

The physician may be tempted, when he encounters anxiety or depression in his patient, to prescribe a tranquilizer or an antidepressant drug without pursuing the diagnostic process further. But symptomatic treatment is no more respectable in the dimension of personality than it is in the treatment of physical illness. Scientific medicine demands that the symptom be traced to its cause, so that the cause may be eradicated.

Psychiatry is still young and is not yet solidly undergirded by a comprehensive psychology in the way that medicine is supported by its basic sciences. Psychology and psychiatry are splintered into numerous sectarian divisions, much as medicine proper was fifty years ago. The physician no longer has to choose whether he will be a homeopath, an eclectic or an allopath. The sects have disappeared as one stable scientific medicine has emerged. The multiplicity of psychologies may similarly be expected to merge into one scientific system as understanding of human personality grows.

Even then, psychiatry can never become wholly scientific, and the psychiatrist must always be more than a scientist. Many neurotic symptoms are traceable to warped attitudes, closely related to the system of values held by the patient. He may suffer, for example, from a sense of guilt, believing that he has done wrong. Science cannot tell him what is right and wrong; this is the province of ethics, a branch of philosophy.

A man may believe that God created the world, a proposition that science can neither affirm nor deny. His belief is an affirmation of faith, a philosophic postulate. Since the patient's beliefs may powerfully influence personality for good or ill, they must be understood and taken into account in treating the whole patient.

The Philosophical Approach in Medicine

The physician is likely to feel very uncomfortable in the realm of philosophy, which may seem to violate his training and cut him adrift from the sciences. A little reflection, however, will make him realize that he has always been dealing with philosophy, just as he has always been "talking prose." Every scientific hypothesis is first a theoretical conjecture. Even when completely corroborated by factual observation, science is underlain by philosophical assumptions about the uniformity of nature and how we may know it. Every simple act of daily living has ethical overtones which are rooted in some basic belief about the nature of man, the existence of God, and their ultimate relationship. These questions may not be as prominent when one is removing a gallbladder or pinning a hip as they are in anxiety or depression; but since they profoundly influence the whole man, they involve every patient and every physician to some degree. Anxiety, depression and personality disorder lead to disturbed attitudes and relationships, which cannot be understood without sharing some understanding of the patient's philosophy of life.

The Judeo-Christian faith is a complete philosophical system that encompasses man's origin and destiny, and that offers an ethical basis for living. Other systems of thought have developed with the coming of the scientific era, but they, too, are only competing philosophies with nothing more than modernity by which to claim superiority.

The Spiritual Dimension

There is still another dimension that the physician must recognize as he seeks to understand and heal the whole man. This is the spiritual dimension.

The Judeo-Christian faith offers not only a philosophy of history and an ethical system, but it tells of a divine-human encounter that has resolved guilt and given new meaning and purpose to existence, and that is open to universal replication. This encounter is an experience, not an intellectual construct. It is an element of existence rather than of philosophy. Such an experience is described by a contemporary in these words:

> More than ever before I am convinced of the reality of a personal God. True, I have always believed in the personality of God. But in the past, the idea of a personal God was little more than a metaphysical category that I found theologically and philosophically satisfying. Now it is a living reality that has been validated in the experiences of everyday life. (King, M. L. "Strength to Love," Harper & Row, 1964. Page 139.)

This experience has been reported by multitudes of persons through many centuries to be an antidote to the futility and meaninglessness of life and to the anxiety of death, and hence has had healing benefit. Any measure with such impressive claims deserves the attention of the physician, who increasingly has had to recognize the baneful effects of anxiety in his patients.

Religion has long been concerned with the spirit. The clergyman has been the specialist

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in this dimension. When the physician concerns himself with his patient's value conflicts and their spiritual experiences, he will find the theologian has already been there a long time. The Judeo-Christian theology not only has a doctrine of man but has ministered to his spiritual needs for centuries. The growing recognition that spiritual problems can produce physical maladies gives new importance to collaboration between clergymen and physicians. Mutual confidence has been slow in developing, especially in the ranks of psychiatry, although the parish minister and the family physician have always been fairly close to each other because they have been close to their people.

The concept of dealing with the whole man not only involves the physician in the philosophic and spiritual dimensions, but it broadens the work of the clergyman as well, bringing him into a closer working relationship with the doctor. In this growing collaboration, the understanding of each can be enlarged. In this cooperation the patient becomes the ultimate beneficiary.

John Wesley had a remarkable insight into this understanding when he wrote these words two hundred years ago:

> Reflecting today on the case of a poor woman who had continual pains in her stomach, I could not but remark the inexcusable negligence of most physicians in cases of this nature. They prescribe drug upon drug without knowing a jot of the matter concerning the root of the disorder and without knowing this, they cannot cure, though they can murder the patient. Whence came this woman's pain (which she would never have told had she never been questioned about it) — from fretting for the death of her son. And what availed medicines while that fretting continued? Why then do not all physicians consider how far bodily disorders are caused or influenced by the mind and in those cases which are utterly out of their sphere call in the assistance of a minister; as ministers when they find the mind disordered by the body call in the assistance of a physician?
> (Wesley Journal, May 12, 1759, IV, 313)

Ladder of Hermes

The Ladder of Hermes was a preparation contrived by Gilbert of England in the thirteenth century. It consisted of 60 simples, compounded by arithmetic progression into one all-purpose prescription: One ounce each of four simples plus two ounces each of four more simples plus three ounces each of four more, etc., until all were incorporated into the final product.

This 15-step Ladder of Hermes was reputed to possess phenomenal potency in curing more than just 15 diseases!

Suspended Animation

The simplest form of suspended animation is that of fainting. When, from the effects of heat or of exertion combined with tight lacing, a young lady becomes pale, and falls down insensible and appears scarcely to breathe, the use of smelling salts is occasionally of service. Though a fainting fit is only the prelude to a fit of hysterics, the patient should be thoroughly roused, and a brisk walk between two not too sympathetic friends will then probably avert a domestic catastrophe.

— Family Physician — Hood Medical Book Co. 1901

A wise man sees as much as he ought, not as much as he can. — Montaigne

History of Medicine

Avicenna, The Prince of Physicians*

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Medically speaking the most influential of the medieval Arabian physicians in the West, Avicenna presents the paradox of being the most widely discussed but the least studied at first hand. He has been called everything from a professional scribbler whose works are a bundle of inanity to the Prince of Physicians. The one safe thing which we can say about him is that he was indeed influential from the 12th to the 17th centuries in Europe, that he transmitted to the West much of the medical theory and practice of the ancient physicians, and that he is still today reverenced as an authority in certain sections of Islam.

A typical, popular biography identifies him as a precocious, 10th century, Persian 'boy-wonder' who mastered metaphysics and logic by his sixteenth year, and who had a renowned reputation in medicine by his eighteenth year. In his adult life, he is typified as a happy-go-lucky, drunken rake in the early hours of the evening, reviving his mental faculties with wine, then meditating in a mosque, indefatigably working on affairs of state all day — all the while grinding out some hundreds of books on everything from medicine to philosophy and psychology. It is said, finally, that he died at the age of 58 of excesses.† If the stories are true, it would be even more remarkable that he could have escaped 'cirrhosis of the brain' long enough to write such an obvious exercise in sustained reasoning as his *Canon of Medicine.* For, whatever else it may be, the *Canon* does have that attribute.

As a physician, Avicenna proposed to deal with two aspects of medicine, the 'speculative' and the 'practical.' He felt that anyone planning to follow his teachings should commit them to memory, even without completely understanding the reasons behind them. He denied that medicine was a 'pure science' or 'speculative only,' and noted that every science has both a speculative and a practical aspect. This division he developed within the traditional Aristotelian distinction between 'potentiality' and 'actuality.' Very much in the same vein as Galen in the *Natural Faculties,* he then noted that the physician should not concern himself with metaphysical questions; but he himself subsequently disregarded the advice by discussing the four traditional elements making up the composition of man, namely: earth, water, air and fire.

Concept of Temperaments

In his concept of temperaments, Avicenna defined them in a manner reminiscent of Galen. Temperament was envisioned as that quality which resulted from the mutual interaction of the four contrary, primary qualities residing within the elements. Temperament was decided by the bal-

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*Avicenna (980-1036 A.D.) or Abú 'Ali Husayn ibn 'Addullah ibn Sina; also called the "Chief Master" or "Second Master," i.e. after Aristotle. Presented before the Society of Medical History of Chicago, January 23, 1963.

**History of Medicine Division National Library of Medicine.

†See particularly S. M. Afnan, Avicenna; His Life and Works, (London, 1958), pp. 62, 68, 76 *et passim;* See also R. Levy, "Avicenna — His Life and Works" in Medical History I, 3, July 1956, p. 249.

Continued

ance of these qualities. After offering eight varieties of temperaments, Avicenna considered the intemperaments, which we might cautiously label 'dyscrasia.' These, in turn, were simple or compound. Each organ or member of the body also had its own temperament, as well as each age, sex, geographical position and occupation. As evolved by Avicenna, these qualities were subdivided into an exhausting number of degrees.

The Humors

His concept of the humors was essentially Galen's. Healthy humor was that moist substance which replaced the loss which the body substance underwent. The residue, or superfluity, was called unhealthy humor. There were four body fluids or humors, namely: sanguineous or hot-moist; serous or cold-moist; bilious or hot-dry; and atrabilious or cold-dry. These, in turn, could be normal or abnormal in varying degrees. Avicenna felt that Galen was wrong in holding all the humors but blood as superfluities; but the reasoning for his disagreement with Galen was purely dialectical, e. g., if the serous humor did not nourish the brain, the brain would not be soft.

(Continued next month)

History of Medicine in Wright County*

As mentioned **Dr. F. A. Atwater** was the first resident dentist to locate in Wright County. He appears first in the Wright County newspapers in June, 1879. However, at first he is mentioned not as a resident dentist but because of his activities as delegate to the National Greenback State Conventions at St. Paul and for his activities as examiner and surveyor of land in the Red River and Northern Pacific Country. In December 1879 he resided at Long Lake but soon after that we find his card in The Eagle of Delano announcing him as "Resident Dentist. Office one door east of the Eagle office . . . Delano." Dentistry apparently did not provide a living as he also ran a clothing store. His store advertisements in the Eagle ended with the following notice: "N. B. Those wishing their teeth filled or extracted will also find my dental chair in readiness in the same place." It seems he experimented with tooth transplantation because in May, 1880 a news item tells that "Dr. Atwater supplanted another tooth this week after it had been extracted." As the year went on, his business affairs seemed to outweigh dentistry. In July, 1880 he became Justice of the Peace of Delano and his wife advertised her readiness to take in boarders; both indicate that extra earnings were needed. Soon he also became an agent for the Manhatten Insurance Company. In September, 1880 he purchased the Clerk House in Minneapolis and left Delano. He kept the Clerk House only eight or nine months, sold it at a good profit and moved with his family to Australia. It cannot be said that he enhanced the dental profession in Wright County. His newspaper ads apparently had the right appeal to the rural areas — they showed a picture of a man greatly suffering from an abscessed tooth.

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*See Minnesota Med 48:1394, 1965.

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Medical Economics

Social Security for Doctors

Under the social security amendments of 1965, physicians and surgeons are brought into the system effective January 1, 1965. Those whose taxable years end on December 31 will pay the required tax on 1965 earnings by April 15, 1966, and annually thereafter by April 15 on their previous year's earnings.

Social security benefits are intended to be a partial replacement of earnings lost because of the worker's retirement, disability, or death. Only income from employment or self-employment counts as earnings under social security. Income from interest, dividends, rentals, sales of property, securities, etc. does not constitute earnings under the social security retirement test.

To be insured under social security and thus qualified for benefits upon retirement requires coverage for a certain minimum number of calendar quarters, depending upon sex and year of birth.

A male doctor born in the year 1897, now 68 years of age, requires 11 quarters of coverage; one born in 1900, now 65 years of age, requires 14 quarters of coverage; one born in 1915, now 50 years of age, requires 29 quarters of coverage; one born in 1935, now 30 years of age, requires 40 quarters of coverage. The intervening ages require comparable quarters of coverage.

Test for Retirement Benefits

Provisions under the retirement test beginning in 1966 include the following: An individual who is otherwise eligible will receive all of his social security benefits if he does not have earnings of more than $1500 in a taxable year. If he earns more than $1500 he loses $1 in benefits for each $2 earned above $1500, but not over $2700. He loses $1 in benefits for each $1 earned over $2700. Upon attaining the age of 72 he can earn all he wishes and still collect all of his social security benefits. Most doctors would earn too much to collect benefits before attaining that age.

A self-employed individual when eligible can receive social security benefits for any month in which he does not engage in a substantial amount of work in his profession or business, regardless of the amount of his annual earnings. As a guide, a self-employed person who works more than 45 hours in a month will be considered to be rendering a substantial amount of service. If he works 45 hours or less, he may be considered retired, depending upon the nature of his profession and the services rendered. If he works 15 hours or less a month, he will always be considered retired and eligible for payment for any such month. Therefore, any doctor eligible for benefits who does not work more than 45 hours in a calendar month should consult the nearest social security office to obtain an evaluation of his social security status.

Whenever benefits are suspended or reduced by reason of excess earnings, benefits to the wife are also suspended or reduced in the same proportion.

Military service prior to the effective date of the social security act, January 1, 1937, is not counted in determining quarters of coverage. Later military service, between September 15, 1940 and December 31, 1956, may be counted under certain conditions, which may be ascertained from the social security office. Active military service performed after 1956 is covered under Social Security. Earnings from military service will not dilute the average monthly earnings and thus reduce benefits, but in most cases doctors will not find their military service to be of any value by way of increasing their social security benefits.

Continued

However, some doctors who do not have enough coverage to be eligible for benefits may become insured by using credit for military service.

All doctors upon attaining age 65, including those who have not worked under Social Security, may apply at the nearest Social Security Office for hospital insurance benefits.

Tax Rates for Self-employed Doctors

The 1965 social security amendments provide tax rates and maximum taxes for all self-employed workers on earnings subject to the tax as follows:

PAYROLL TAX

	SELF-EMPLOYED WORKER	
	Tax Rate	Maximum Tax
1965 tax on first $4800 of yearly earnings	5.4 %	$259.20
Tax in future years — on first $6600 of yearly earnings:		
1966	6.15%	405.90
1967-68	6.40%	422.40
1969-72	7.10%	468.60
1973-75	7.55%	498.30
1976-79	7.60%	501.60
1980-86	7.70%	508.20
1987 and thereafter	7.80%	514.80

Monthly and Maximum Benefits

Assuming that the doctor earned $6600 annually from the first year of coverage beginning January 1, 1965, until retirement at age 65, or as soon thereafter as qualified, his monthly benefits would be approximately as follows:

Present Age	Qualifying Age	Monthly Benefit	Wife's Benefit	Total
68	71	$101.70 (sic)	$50.90	$152.60
65	69	96.30 (sic)	48.20	144.50
50	65	121.00	60.50	181.50
30	65	166.00	83.00	249.00

The male doctor born in 1897, now 68 years of age, could increase his social security benefits to a maximum by working as follows:

Through 1968	$122.00	$61.00	$183.00
Through 1969	143.00	71.50	214.50
Through 1970	163.00	81.50	244.50
Through 1971	168.00 (Max.)	84.00	252.00

A male self-employed doctor born in the year 1900, now 65 years of age, could increase the above monthly benefit of $96.30 by continuing to work beyond the minimum 14 quarters required for coverage. Assuming he continued to earn at least $6600 annually, his monthly benefits, with a possible maximum of $168.00, would be as follows:

	Monthly Benefit	Wife's Benefit	Total
Through 1969	$110.30	$55.15	$165.45
Through 1970	124.20	62.10	186.30
Through 1971	138.00	69.00	207.00
Through 1972	151.00	75.50	226.50
Through 1973	164.00	82.00	246.00
Through 1974	168.00 (Max.)	84.00	252.00

Maximum benefits for other ages which have not been detailed here can be obtained if the doctor works a few years beyond his sixty-fifth birthday. A table of details can be obtained from the social security office, but from the tables given in this manuscript a fairly adequate extrapolation would provide the figures.

In these illustrations only the 68, 65, and 50-year-old doctor can increase his benefits by continuing to work for a few years beyond his sixty-fifth birthday. The 30-year-old doctor, continuing to pay his social security tax, cannot appreciably increase his benefits after the age of 65, even though he continues to work and earn until the age of 72.

No doctor can collect his social security benefits and at the same time earn $6600 or more until he attains the age of 72, when he can then earn as much as he wishes and also collect the maximum social security.

Social Security vs. Life Annuity

It might be of some interest to compare the total monthly benefits for a 72-year-old married couple with the amounts obtainable from a commercial life annuity of similar type, if funds equal to the amount of social security taxes required under the present law could be accumulated in a savings account at 4 percent compounded annually, and invested at retirement in a life annuity. In this illustration income taxes on the savings account earnings have been ignored:

		Combined Monthly Annuity for Life No Principal Remaining		
	Funds Accumulated to Age 72	Social Security	Commercial Insurance	Life* Expectancy Age
From age 68	$ 1,704.00	$252.00	Nominal	81.08
From age 65	3,548.00	252.00	Nominal	80.01
From age 50	16,572.00	252.00	$136.40	76.23
From age 30	54,758.00	252.00	450.71	74.61

*American Table for 1949

The above annuities would be allocated between husband and wife at age 72 in the same proportion as the comparable social security benefits.

The 30-year-old doctor in the above table under the commercial annuity, for example, would receive a monthly life annuity of $300.47; his wife would receive one half of this amount while both were living, making a total of $450.71, and if she survived her husband her monthly annuity would be 82½ percent of his, or $247.89. Under social security she would receive $135.00 per month.

From these figures it is obvious that doctors older than 50 years of age can increase their social security benefits by continuing to earn and to pay the social security tax until maximum benefits are attained.

The 30-year-old doctor would come out about even if he retired at age 65. If he continued to work until age 72, earning $6600 a year and thus receiving no social security benefits until then, he and his wife would have to live to the age of 90 to recover in benefits, at the maximum rate of $252.00 per month, his social security contributions of $54,758. On a commercial life annuity at age 72, however, he and his wife could live out their lives handsomely on $450.71 a month as long as they live, with a life expectancy to 82.7 years.

The Advantages of Social Security

It provides an annuity for a doctor now older than 50 who at age 72 can receive greater benefits than from a comparable amount of saved income. In addition, it permits a doctor to retire as early as age 62 with a reduced benefit.

It provides hospitalization for doctors age 65 or older. It provides disability benefits if a doctor becomes unable to work before age 65. It also provides survivors' benefits to a doctor's widow and to his children if they are still young, up to a maximum of $368.00 a month.

For the doctor now 30 years of age it provides in effect an enforced savings comparable to a life annuity at age 65 from a commercial insurance company, if he continues to earn $6600 and receives no benefits until age 72.

Disadvantages of Medicare

For the doctor who has the ability to save consistently from the beginning of his career until age 65 or later, it's not a bargain.

It does not provide adequately for catastrophic medical or surgical illness.

Social security taxes and benefits in the above illustrations are those provided under the social security amendments of 1965. If the past is any guide to the future, however, it is highly probable that both the taxes and the benefits will be increased with the passage of time. What the 30-year-old doctor may be spending for and receiving from social security 40 years hence remains to be seen.

The figures on savings account accumulations and on life annuities were obtained from the Northwestern Life Insurance Company. The figures on social security taxes and benefits were provided by the local social security office, which should be consulted for any detailed information desired.

Medicare Law Provisions, Benefits Outlined

Medicare, formerly known as H.R. 6675, is now Public Law 89-97 or the Social Security amendments of 1965. Having been passed by the House of Representatives and Senate and signed by the President, Medicare has become a matter of vital importance to the physician and his patient.

While the scope of Medicare has not yet begun to unfold and many questions still remain unanswered at this time, certain facts are definite. These have been summarized in a pamphlet "Your New Health Insurance" published by the United States Department of Health, Education and Welfare. Copies of this publication and an application card are

Continued

being mailed to everyone 65 or over who is eligible for Social Security benefits and to beneficiaries who will be 65 years of age soon. The mailing is expected to be completed by the middle of December, 1965.

Following is the text of "Your New Health Insurance" reprinted for your information.

Your New Health Insurance

The Social Security Amendments of 1965, which were signed into law by President Johnson on July 30, provide two different kinds of health insurance for people 65 or older.

- *Hospital Insurance,* which will pay most of the cost of hospital services and certain other posthospital expenses.
- *Medical Insurance,* which will help you pay much of the cost of doctors' services and certain other medical expenses.

Since you are 65 or will be before July 1966 and are entitled to social security or railroad retirement benefits, you will automatically be covered by the hospital insurance program. You will be covered by the medical insurance program only if you apply for it. In order to get this protection, you should fill in and return the enclosed card.

Important!

Do not because of this new law cancel any hospital insurance or medical insurance you may already have. The hospital insurance and medical insurance under the Social Security Act do not begin until July 1, 1966.

Your Hospital Insurance

All social security beneficiaries 65 or over are automatically entitled to *Hospital Insurance* benefits and need not take any action.

What Services Are Covered?

Beginning in July 1966, the hospital insurance program will pay the cost of covered services for the following hospital and posthospital care:

- Up to 60 days in a participating hospital (except for the first $40) and all but $10 per day for an additional 30 days for each spell of illness.* (There is a lifetime limit of 190 days for treatment in mental hospitals.)
- Up to 20 days in an extended care facility (a qualified skilled nursing home or a convalescent section of a hospital) and all but $5 per day for an additional 80 days for each spell of illness* You must have been in a hospital for at least 3 days before these benefits are payable. (This part of the program begins on January 1, 1967.)
- Up to 100 home-health visits by nurses or other health workers from qualified home health agencies (but not doctors) in the 365 days following your release from a hospital after a stay of 3 days or more, or from an extended care facility.
- 80% of the cost of outpatient diagnostic tests in a hospital (after you pay the first $20) for each 20-day period of diagnostic testing.

For services in a hospital or extended care facility, benefit payments will cover the cost of services in semi-private accommodations plus the cost of drugs, supplies, and most services customarily furnished by the institution.

What Services Are Not Covered?

No payment will be made under hospital insurance for the services of physicians, including the services of anesthesiologists, radiologists, physiatrists and pathologists. (The supplementary medical insurance program, however, does cover physicians' services). Payment will not be made for private duty nurses, custodial care, or for items furnished for the patient's convenience.

Payments will ordinarily be made under the program only in the 50 States, the Commonwealth of Puerto Rico, the Virgin Islands, Guam, and American Samoa. Hospital services under the basic hospital insurance plan may be provided in border areas immediately outside the United States if comparable services are not accessible in the United States for a beneficiary who becomes ill or is injured in this country.

Your Health Insurance Card

You will receive through the mail a health insurance card shortly before July 1, 1966.

When your doctor arranges for you to receive services covered by your hospital insurance, show your health insurance card to the hospital, extended care facility, or home health agency which is to provide the services. The hospital insurance program will pay for the covered services you receive as described on pages 2 and 3 of this leaflet. If you enroll in the medical insurance program described below, your health insurance card will show that you are also entitled to the services covered under that program.

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*A "spell of illness" begins on the first day you receive covered services as a patient in a hospital or extended care facility. It ends after you have been out of a hospital or extended care facility for 60 consecutive days. You may be discharged and readmitted several times during a spell of illness, but a new spell of illness cannot begin until you have not been a patient in any hospital or extended care facility for 60 consecutive days.

Your Medical Insurance

Medical insurance is voluntary, with both you and the government sharing the cost equally. To get this insurance when the program begins, you must apply for it by March 31, 1966.* Please fill out and mail the card even if you do not want medical insurance, so that we may be sure that you have had an opportunity to consider the medical insurance plan. If you decide to take medical insurance, $3 a month will be deducted from your benefit checks beginning with the check you receive in July 1966. You do not pay any cash.

What Does Medical Insurance Cover?

Beginning in July 1966, the medical insurance program will help you pay for the following medical services:

- Physicians' and surgeons' services in the hospital, doctor's office, home, or elsewhere.
- Up to 100 home health visits under an approved plan each year with no need for prior hospitalization. This is in addition to the 100 visits provided under the hospital insurance program.
- A number of other medical and health services, such as diagnostic services, X-ray or other radiation treatments, surgical dressings and splints, casts, and rental of medical equipment.

Does Medical Insurance Pay the Full Cost of These Services?

No. You pay the first $50 in each calendar year for these services. Your medical insurance then pays 80% of the reasonable charges** for additional services. For example, if your covered medical bills were $500 in a year, the program would pay $360. Your medical insurance pays only for services you receive beginning with July 1966. No expenses you have before that time can count toward the $50 you pay.

What Is Not Covered?

Medical insurance does not cover some services such as the cost of routine physical check-ups, drug prescriptions, eye glasses, hearing aids, and ordinary dental treatment. It does not cover services received outside the United States (except for Puerto Rico, the Virgin Islands, Guam, and American Samoa).

How Do You Pay for Medical Insurance?

If you are receiving social security payments, you will not pay any cash; your $3 premium will be deducted from your social security check beginning with the check you receive in July 1966 and your insurance will begin with that month.

If you are not eligible for social security checks for one or more months, you will be informed how to continue your insurance.

The law provides that the $3 premium rate will be continued through 1967.

In each odd-numbered year beginning with 1967, the cost of the medical insurance program will be studied. If the premium rate, including the government's share, is not enough to cover the cost of the program for the next two years, the rate may be changed. The government will continue to pay half the cost.

When you enroll for medical insurance, you are not under any obligation to continue it beyond the end of the next odd-numbered year. Thus, if there is at any time an increase in the premium rate, you will at the same time have an opportunity to drop out of the program if you wish.

If You Decide to Drop This Insurance

If your premiums are being deducted from your social security benefits and you decide to drop out of the medical insurance program, you may do so during the last quarter of any odd-numbered year.

If you do drop out, you may re-enroll once,

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*If you will reach 65 in January 1966 or later, your first enrollment period will end 3 months after the month in which you reach 65.

**For services provided by an organization on a prepayment basis and for certain other services, the medical insurance may pay 80% of the reasonable cost rather than 80% of the reasonable charges.

but only during the last quarter of an odd-numbered year and only if you re-enroll within three years after you dropped out.

What You Will Lose If You Enroll Late

There are several good reasons for signing up for the medical insurance program during your first enrollment period. If you pass up your first opportunity, you will not have another chance to sign up until the next general enrollment period (October 1, 1967, to December 31, 1967). Furthermore, if you wait to enroll, you may have to pay a higher premium for the same protection; and your coverage will not begin until 6 to 9 months after you enroll.

These provisions take into account the higher cost of insuring a person who does not enroll and begin paying premiums at his first opportunity.

If You Cannot Meet Your Medical Expenses

The health insurance programs will pay a large part of the cost of health care for most older people, but they do not pay the entire bill. If you have medical expenses you cannot pay, you may qualify for aid from your public welfare agency. Most States have medical care programs for aged people who cannot pay their medical bills and the 1965 Amendments make it possible for the States to strengthen and improve these services. Your public welfare agency may be able to help you.

The Venous System in Ancient Egypt

In the Heart are the vessels to the whole of the body.

There are four vessels to the Nostrils, two of which convey mucus and two blood.

There are four vessels in the inside of either Temple.

There are four vessels which divide in the Head and spread out in the back thereof.

There are four vessels to his Ears, two to the Right side and two to the Left. Breath-of-Life goes in the Right Ear and Breath-of-Death into the Left.

There are six vessels that run to the Arms, three to the Right and three to the Left, and they lead right down to the Fingers.

There are six vessels that lead to the Feet, three to the Right and three to the Left. They reach down to the Soles of the Feet.

There are two vessels to his Testicles which convey the Semen. There are two vessels to the Kidneys, one to one Kidney, the other to the second Kidney.

There are four vessels to the Liver which convey to it Moisture and Air.

There are four vessels to the Intestines and to the Spleen which likewise convey Moisture and Air. There are two vessels to the Bladder which convey the Urine.

There are four vessels which end in the Rectum. They give and bring forth in it Moisture and Air. Afterwards they turn towards the Rectum, each vessel to the Right and Left side right down to the Feet, mixing itself with the excrement.*

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*Bryan, Cyril: The Papyrus Ebers, D. Appleton and Company, New York, 1931, p. 124.

Meetings and Announcements

The same corrupt dispositions which incline men to sinful ways of getting will incline them to the like sinful ways of spending. — M. Henry

NOVEMBER

Inaugural Scientific Program of the new Ancker Hospital, St. Paul, will be held November 11-13. Program will include two days of general medical meetings. Contact: James F. Hammarsten, M.D., Ancker Hospital, St. Paul.

Wisconsin Society of Pathologists Meeting, November 13-15, Pathology Department, Marquette University, School of Medicine, Milwaukee. Contact: Joseph L. Teresi, M.D. at 561 North 15th St., Milwaukee.

Annual Meeting of American Society for Colposcopy and Colpomicroscopy, New York City, Hotel Americana, November 6-7. Contact: Fritz Beller, M.D., New York University School of Medicine, 550 First Avenue, New York City.

Seventh National Conference on Medical Aspects of Sports, November 28-December 1, Philadelphia, Benjamin Franklin Hotel. Contact: Secretary, 535 North Dearborn Street, Chicago.

American Society of Cytology Meeting, Statler-Hilton Hotel, New York, New York, November 4-6. Contact: Warren Lang, M.D., 1012 Walnut Street, Philadelphia.

Committee on Injuries of the American Academy of Orthopaedic Surgeons will present a comprehensive postgraduate course on the Treatment of Injuries in Dallas, Texas, Marriott Motor Hotel, November 17-20. Contact: Sam Banks, M.D., 29 E. Madison Street, Chicago.

National Society for Crippled Children and Adults Convention, November 19-22, Palmer House, Chicago. Contact: Society, 2023 West Ogden Avenue, Chicago.

Zumbro Valley Medical Society annual meeting, November 3, 8:00 p.m., Mann Hall, Rochester. Election of officers.

Minnesota Surgical Society business and scientific program, 9:00 a.m. to 5:00 p.m., November 5, Minneapolis.

Minnesota Academy of Medicine meeting 6:30 p.m., November 10, Town and Country Club, St. Paul.

St. Louis County Medical Society executive committee meeting, 6:00 p.m., November 11, and regular meeting at 8:00 p.m., St. Mary's hospital, Duluth.

Minnesota Society of Clinical Pathologists Tumor Seminar and meeting, 9:00 a.m. to 4:30 p.m., November 13, Minnesota Club of St. Paul.

Twin City Urological Society meeting 6:00 p.m., November 19th, Town and Country Club, St. Paul.

Southern Minnesota Academy of General Practice meeting, November 23, 4:00 p.m., Mankato.

Ramsey County Medical Society meeting 8:00 p.m. November 29, 1500 Lowry Medical Arts Building, St. Paul.

Conference on Medical Aspects of Physical Activity, November 12 and 13, Richfield High School in Richfield. Contact: Lyle Lewis, Richfield Public Schools, Richfield, Minnesota.

Mount Sinai Hospital Medical Center of Chicago symposium on the Management of Chronic Disease Patient. November 3 and November 17th. Contact: Aaron M. Rosenthal, M.D., Mt. Sinai Hospital in Chicago.

Fifth Annual Milwaukee Medical Conference, November 11-13, at Coffey Auditorium of Milwaukee County Hospital. Contact: Medical Society of Milwaukee County, 756 N. Milwaukee Street, Milwaukee, Wisconsin.

ANNOUNCEMENT

Cardiopulmonary Seminar at Mount Sinai Hospital, Minneapolis, November 11 and 12. Seminar will be devoted to function tests of heart and lung. Seminar sponsored by Hennepin County Medical Society, Minnesota Heart Association, and Minnesota State Board of Health. Seminar has been approved in the past for fifteen hours of postgraduate study by the American Academy of General Practice. Contact: Jerome Grismer, M.D.; Mt. Sinai Hospital in Minneapolis, Minnesota.

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Minnesota Heart Association and American College of Cardiology Symposium, December 4 (one day) at the Sheraton-Ritz Hotel in Minneapolis. Subject will be: "Adrenergic Blocking Agents with Special Reference to Hypertension and the Catecholamines." Contact: Executive Secretary of American College of Cardiology, 9650 Rockville Pike, Washington, D.C. or the Minnesota Heart Association Office in St. Paul.

The Pharmacopoeia of Ancient Egypt

A glance through the pharmacopoeia on which the Papyrus Ebers is based is not to be undertaken lightly. To be sure we encounter there a number of drugs that figure in our pharmacopoeia today, but they are dwarfed by the weird and wonderful substances that the Scribe gravely transcribes. It is here that we first make acquaintance with that God-given drug, Castor Oil, which besides finding itself in a hundred prescriptions has the honour of a special mention in the body of the book:

"*Memorandum on the Use of the Castor Oil Tree (As Found in the Ancient Writings of the Wise Men)*

When a Person rubs its Stalk in Water and applies it to a Head which is Diseased, he will immediately become as if he had never been ill.

When a Person who suffers from Constipation chews a little of its Berry along with Beer, then the Disease will be driven out of the Sick One's body.

Furthermore, the Oil from its Berries is pressed out as an Ointment for the use of any Person who has the uha-abscess-with-stinking-matter. Lo, the Evil will fly as though he had suffered nothing! For Ten Days he anoints himself afresh daily in the morning in order to drive the abscess away.

But extolled though it was these ancient physicians were not satisfied with Castor Oil alone, and in their search for the wherewithal to fight the disease which afflicted the land they reached as high as the heavens, actually prescribing Excrement-of-the-Gods. They laid heavy hands on the animal world, on the mineral world, on the plant world, and not least on the World of Fancy; and having got a substance which they imagined possessed the slightest therapeutic virtue they prescribed it internally and externally, raw and cooked, ripe and unripe; in some cases over-ripe and actually rotting.*

Their ingenuity not yet exhausted, they turned their attention to the administration of the remedies, exhibiting again a versatility in every way comparable to their pharmaceutical efforts. Thus, we read of the mother who was instructed to spit the remedy into the child's mouth, of the woman who was ordered to take her medicine while she sat cross-legged, and of that other lady who, after chanting the Magic Formula, was told to have coitus before swallowing the medicament.

A final reference must be made to the vehicles by which it was sought to make the nauseous mixtures and objectionable messes which passed for poultices less nauseous and less objectionable. These vehicles, Beer, Milk, and Water, were employed with well balanced impartiality; they were often to be found in the same concoction; they appear in all sorts of forms, recognizable and unrecognizable. Thus Beer, a favourite vehicle, was prescribed as Plain Beer, Sweet Beer, Bitter Beer, Cold Beer, Warmed Beer, Flat Beer, Yeast-of-Beer, Froth-of-Beer, Beer-which-has-been-Brewed-from-many-Ingredients; while in a bright moment they bethought themselves of Swill-of-Beer. Milk also afforded them some scope; it appears as Fresh Milk, Sour Milk, Spoiled Milk, Cooked Milk, Ass's Milk, Cow's Milk, Man's Milk, Milk-of-a-Woman, Milk-of-a-Woman-who-has-borne-a-Son, Milk-of-the-Sycamore, and Milk-juice. As for Water, we find Plain Water, Well Water, Spring Water, Salt Water, Mineral Water, Cake Water, Linseed Water, Natron Water, Water-from-the-Bird-Pond, Water-from-the-Rain-of-the-Heavens, and Water-in-which-the-Phallus-has-been-washed!"*

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*Bryan, Cyril: The Papyrus Ebers, D. Appleton Company, New York, 1931, p. 15.

Classified

Classified advertising rates are twenty (20) cents a word; minimum monthly charge $5.00; key number, fifty (50) cents additional.

Replies to advertisements with key numbers should be mailed in care of MINNESOTA MEDICINE, *496 Lowry Medical Arts Bldg., St. Paul, Minn. 55102*

PHYSICIAN — TB and Geriatric State Hospital; accredited; $12,828.00-$15,600.00 based on qualifications and experience; desirable suburban location; residence available; liberal sick leave and vacation benefits; excellent retirement system. Contact: Medical Director, Glen Lake State Sanatorium, Minnetonka, Minnesota.

LOCUM TENENS in internal medicine wanted by competent third year medical resident. Three weeks in November or December. Contact: MINNESOTA MEDICINE — 329, 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED GENERAL PRACTITIONER able to do some surgery. Present physician retiring after 49 years. Good community, prosperous farming. Good schools and churches. New hospital. Contact: MINNESOTA MEDICINE — 330, 496 Lowry Medical Arts Building, St. Paul 55102.

TWO G.P.'s NEEDED — Northern Minnesota county seat. New hospital, office space available, two other physicians in town, anesthetist on hospital staff, good schools, all churches, excellent hunting and fishing, housing available. Full details upon request. Contact: Administrator, Roseau Area Hospital, Roseau, Minnesota.

GENERALIST NEEDED. Death of associate in three-man group in general practice in White Bear Lake, Minnesota, requires immediate replacement. Salary with advancement to partnership negotiable. Excellent opportunity for young man in an established practice of young men (under 38 years old). New building in suburban area of St. Paul. Locum tenens also considered. Call or write: A. J. Rushay, M.D. or T. G. Briggs, M.D., 777-1341

WANTED LOCUM TENENS. Doctor desires generalist to work for month of February 1966 in one (1) doctor clinic. Write Brainerd Clinic, Box 408, Brainerd, Minnesota.

BADLY NEEDED — G.P., Internist or Surgeon to associate with two-man G.P. partnership. Unapposed territory. New hospital, nursing home, children's home! Superb hunting, fishing, golf, pool, winter arena. Progressive town! Delmore Clinic, Roseau, Minnesota 56751.

A 13 MEMBER specialty group in the Midwest will need several men to replace and add to present staff. This has been a rewarding group for years, is now, and will be for years to come. We need 3 internists, 1 dermatologist, 1 ob-gyn, 1 pediatrician, 1 general and thoracic surgeon, 1 orthopedist, 1 ophthalmologist, 1 otorhinolaryngologist, and 1 psychiatrist. This is a very good town for a family man. Three colleges (1 a State College). Good schools and excellent recreation programs. Good hunting, fishing and water sports. Applicants should be board certified or completing requirements. Write MINNESOTA MEDICINE — 324; 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED: Board Certified or eligible internist to associate with group in large, active practice in Minneapolis. Group consists of Surgeon, Obstetrician, Pediatrician and Internist maintaining downtown and suburban offices. Partnership in mind. Contact: Jesse J. Barron, M.D., 1127 Medical Arts Building, Minneapolis, Minnesota 55402, FEderal 2-8259.

FOR RENT: Successful medical building. Opportunity for doctor to start new group. Rent at less than $3.00 square foot. Deluxe, modern, air-conditioned, all brick building with capacity up to four doctors. Located at 36th Avenue North and Noble Avenue in Northwest Suburban Minneapolis. For further information: Call Noble Drug at 588-9449 and ask for Ben or Lou.

MORGAN, MINNESOTA, Wants General Practitioner — present physician retiring after 33 years. Opportunity to take over well established practice. Progressive community in the best rural area of Southern Minnesota. Office space and equipment available. Call or write John Hageman, Pharmacist, Morgan, Minnesota. Telephone Morgan No. 96.

WHITE BEAR LAKE, MINNESOTA. A suburban community of 35,000 and growing fast. Available several ground floor air-conditioned suites in fireproof building in central business district, free municipal parking lot at second entrance in rear. See: N. R. Dittberner, 316 Washington Avenue, White Bear Lake. Telephone: Collect anytime 429-7787.

BUSY, GROWING aggressive 3-man partnership in Northwest Wisconsin serving a trade area of 15,000 needs a well-trained recent graduate with fulfilled military obligations to associate immediately on excellent salary, with partnership in 1 year if mutually agreeable. Modern 15 room air conditioned brick clinic building is being doubled in size this year. 32 bed hospital and new 42 bed nursing home one minute from clinic. New 1500 student consolidated school. Excellent hunting, fishing and outdoor sport facilities in immediate area. Contact: MINNESOTA MEDICINE — 317; 496 Lowry Medical Arts Building, St. Paul 55102.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE — 289; 496 Lowry Medical Arts Building; St. Paul, 55102.

WANTED: Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty seven bed hospital, X ray and laboratory technicians and nurse anesthetist. Good

Continued

hunting and fishing. Adequate salary and time off. Contact: A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

PROFESSIONAL AIR AMBULANCE. Multi or single engine aircraft. All weather and night flight capability, anywhere in the U. S. Oxygen, Respirator, Aspirator, Nursing service, all medications. Also full time M.D. Board Anesthesiologist providing all medical care in flight available on request. MIDWEST AIR TRANSPORTS, Operations Office, Municipal Airport, Waterloo, Iowa, Phone 319-2331083.

OFFICE SPACE now available in busy Bloomington. 713 square feet of new space in building with busy group of G.P.'s, dentist and suburban OB-GYN office. Ideal for ophthalmology, ENT or pediatrics. 8040 Penn Avenue South. 888-9211.

PART TIME INTERNIST OR GENERAL PRACTITIONER. Good compensation — Midway Area. Alfred F. Anderegg, M.D.; 2500 Como Avenue, St. Paul, Minnesota.

WANTED INTERNIST, Board qualified or certified for 22-physician mixed group of general practitioners and specialists (East Range Clinic, Virginia, Minnesota). Salary first year, then full partnership. Centrally located in area of rapidly expanding economy.

WANTED: one or two general practitioners. Excellent clinic and hospital facilities. Rural practice established 18 years. Salary open, partnership if compatible. Lloyd H. Klefstad, M.D., Greenbush, Minnesota.

SACRED HEART, MINNESOTA, doctorless since 1961, wants general practitioner. Population 700, accredited hospital 10 miles away. Write: Rev. Robert Bardy, Phone 765-2547, Sacred Heart, Minnesota.

A THREE MAN group needs a fourth general practitioner in a fast-growing West St. Paul area. Begin with salary and join partnership with full participating advantages. Write: MINNESOTA MEDICINE — 326, 496 Lowry Medical Arts Building, St. Paul 55102.

FOR SALE: Family practice in community just outside of Minneapolis. Ten minutes to 100 bed hospital. Full privileges assured. Finances no problem. Write: MINNESOTA MEDICINE — 327, 496 Lowry Medical Arts Building, St. Paul 55102.

MEDICAL ART. Drawings, charts and lettering for publication, slide lectures, movies, exhibits and television. Also three dimensional models. Al Hage — 339-1012, Minneapolis.

GENERAL PRACTITIONERS — one or two wanted by two local physicians and community. Progressive community in heart of good farming section of Central Minnesota. Community owned 34-bed hospital with 45-bed nursing home wing. Excellent grade and high schools; good hunting and fishing area; golf course and other recreational facilities near by. For further information, contact Administrator Melrose Hospital, Melrose, Minnesota.

MIRACLE MILE MEDICAL CENTER: St. Louis Park has doctor's office available. This modern medical space features elevator service, air conditioning, plus plenty of parking. Call or write: Roger Wahldick at Draper and Kramer, Inc. FE 9-9441, Minneapolis.

CHIEF OF PSYCHIATRIC SUPERVISORY STAFF needed to help with clinical supervision and teaching in expanding (18 resident physicians) fully approved residency training program. Ideal living in active community in the heart of Michigan's Water Winter Wonderland. Newly established position requires board certification in psychiatry and additional experience in clinical supervision. Salary range depending upon qualifications, $17,393 to $21,339. Unparalleled Michigan civil service benefits. Contact Arthur F. Dundon, M.D., Clinical Director, Traverse City State Hospital, Traverse City, Michigan. An equal opportunity employer.

GENERAL PRACTITIONER WANTED: to associate with physician-surgeon in Owatonna, a Southern Minnesota community, 25,000 population. Clinic building three years old; with five large treatment rooms, lab.; x ray; central supply; two doctors' offices; pharmacy; and business offices. Located next door to 85 bed city hospital. Good opportunity for partnership. Contact: O. W. Roberts, M.D.; 920 South Cedar Street; Owatonna, Minnesota. Phone 451-4630.

GENERAL PRACTITIONER WANTED to be associated with 40-year old general practitioner. Winona, Minnesota. Excellent practice conditions. 3.5 million dollar hospital. Write: MINNESOTA MEDICINE — 322; 496 Lowry Medical Arts Building, St. Paul 55102.

LOCUM TENENS wanted for general practice in St. Paul from mid-February through March, 1966. Write: MINNESOTA MEDICINE — 328; 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED: physician under 35 to assist, then share busy general practice in Long Island area of metropolitan New York with young GP. Must have or be eligible for New York license, be able to do uncomplicated OB and assist at surgery. Salary first year, then increasing percentage to full partnership. Write: Ralph E. Schlossman, M.D., 130 Lefferts Blvd., South Ozone Park, L. I., New York.

GENERAL PRACTICE Minnetonka, 20 minutes from Minneapolis loop. Ideal location for solo start with expansion to clinic. New building. Hospital nearby. Good parking. Dentist now located in one wing. Call or write: Cliff Kommedahl, 12401 Minnetonka Blvd., Minnetonka, Phone 935-8247.

GENERAL PRACTITIONER FOR PERMANENT POSITION — salary open, under thirty-five years of age, partnership agreement negotiated in 18 months, scheduled post graduate and vacation periods. New Modern medical-dental clinic with full diagnostic facilities at High 100 and Wayzata Blvd. Large established family practice with opportunity for surgical privileges. Contact: Alton C. Olson, M.D.; 5250 Wayzata Blvd., Minneapolis, Telephone 545-1661.

By communicating our grief we have less, by communicating our pleasure we have more. — Greville

INTERNIST wanted to join specialty group. Growing practice in Central Minnesota Lake Region. New modern clinic. Group includes a Pediatrician, Surgeon, Obstetrician and Internist. Write: Dr. John O'Leary, Northland Clinic, Brainerd, Minnesota.

GENERAL PRACTITIONER AVAILABLE. Completing military June, 1966. Five years experience; married, desires group practice Rochester, Minneapolis, St. Paul or surrounding area, minimum OB and surgery. Write MINNESOTA MEDICINE — 331, 496 Lowry Medical Arts Building, St. Paul, Minnesota.

WANTED: young general practitioner to join six-man group consisting of 4 GPs, a general surgeon, and radiologist. College town of 5,500, 30 miles from Twin Cities. Also need LOCUM TENENS in general practice. Contact: Ed Jenkins, Mgr., River Falls Medical Clinic, River Falls, Wisc. Phone 425-5322.

WANTED — Internist, board certified or qualified, to associate with two board certified internists. Ten man multi-specialty group. (Lenont Peterson Clinic, Virginia, Minnesota) — Heart of the expanding taconite industry.

MEDICAL TECHNOLOGISTS — positions available for ASCP registered or eligible technologists. Excellent salary and fringe benefits. Apply Ancker Hospital, 495 Jefferson Avenue, St. Paul, Minnesota.

WANTED locum tenens for month of February 1966. Can live in my home. If married, bring wife and children. Modern hospital and clinic, consultation available. Contact as soon as possible by mail or telephone: Wm. C. Heiam, M.D., Cook, Minnesota. Telephone: 666-3354 or 666-2261.

PHYSICIAN (General Medicine or Surgery) at 245 bed VA General Hospital in scenic Black Hills. Area offers excellent hunting, fishing, recreation. Requirements: Graduate approved school, citizenship, license any state, salary based on qualifications, housing available. Nondiscrimination in employment. Contact Chief of Staff, VA Center, Hot Springs, South Dakota 57747.

MEDICAL SUPERINTENDENTS top administrative positions in a challenging program. The Michigan Department of Mental Health is now considering candidates to fill current vacancies as Medical Superintendent. Positions are available in facilities for the retarded and the mentally ill. Applicants must have had five years of responsible administrative experience in the field of medicine. Three years of experience in the field of mental health is required. Additional recognition will be given for medical specialty boards. These openings present a unique opportunity to participate in one of the most dynamic mental health programs in the country. Our state hospitals are participating in the community mental health center program as well as training and research activities. Salary up to $25,307 depending upon qualifications. Housing available on grounds. Outstanding fringe benefits provided under the Michigan Civil Service. Apply to: Robert A. Kimmich, M.D., Director, Michigan Department of Mental Health, 5301 — Lewis Cass Building, Lansing, Michigan. An equal opportunity employer.

FOR SALE — Almost new office equipment, waiting room furniture, examining tables etc. for depreciated value. Easy terms. Write: MINNESOTA MEDICINE — 332, 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED: Psychiatrist and general physician for full time staff positions in private psychiatric hospital currently in process of increasing range of inpatient and outpatient services. Midwest metropolitan area. Private practice opportunities after one year. Salary open according to qualifications. Attractive working conditions. Fringe benefits. Write: MINNESOTA MEDICINE — 333, 496 Lowry Medical Arts Building, St. Paul 55102.

FOR SALE: Established general practice with 97% collections. Town of 7,000 with fifty-bed hospital. Almost-new offices for rent without lease unless desired. Your cost. Depreciated value of equipment — all less than five years old. Write: MINNESOTA MEDICINE — 334, 496 Lowry Medical Arts Building, St. Paul 55102.

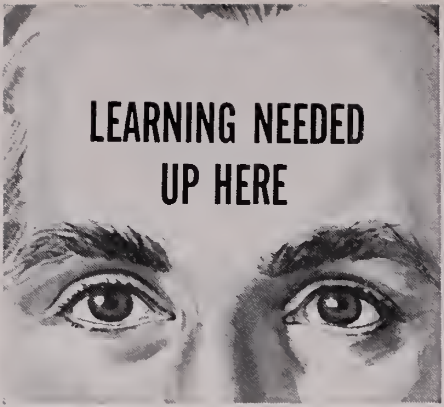
WANTED SOMEONE in East Side St. Paul general practice who would desire temporary locum tenens, one, two or three months. Write: MINNESOTA MEDICINE — 335, 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED: Generalist desiring fast start in too busy St. Paul practice. No covenants or contingent clauses. You move to available nearby independent office facilities as soon as you establish an adequate following of your own, or you stay as a partner if you desire. Incidentally lousy working conditions: new building, built-in Hi-fi, every third week off. If you desire to establish yourself permanently in present location. You name your own terms. Write MINNESOTA MEDICINE — 336, 496 Lowry Medical Arts Building, St. Paul 55102.

Astrology and Medicine

In the broad and baffling spectrum of human maladies distant Uranus is responsible for such ailments as ruptures, strictures, cramps, and spasms — besides hallucinations and some other psychic disturbances. Neptune, still more remote from earth, is culpable for such obscure and unresponsive disorders as comas, hypochondriasis, somnambulism, and drug addiction. Both Uranus and Neptune have an aura of mystery and other-dimensionalism.

Democracy is based upon the conviction that there are extraordinary possibilities in ordinary people. — H. E. Fosdick



Who will do it? The colleges of course! They educate leaders to meet the challenges America faces in business, science, government, everyday living.

But the colleges need help. Quality education is expensive, and more Americans require a college education.

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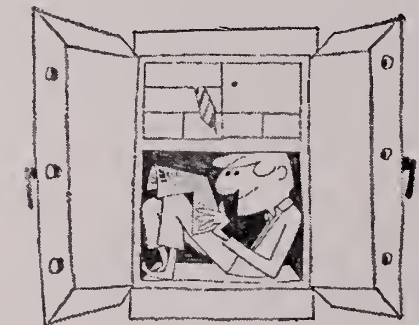
the first thing to save for your old age is you!



Put first things first. Form the *life*-saving habit. Have a health check-up once a year, every year. That way your doctor has the chance to detect cancer in its early and more curable stage. Start your new saving plan now, with a phone call to your doctor!

american cancer society

THIS SPACE CONTRIBUTED BY THE PUBLISHER

Anturane®
brand of
sulfinpyrazone

Dosage
Anturane, brand of sulfinpyrazone, is available as white, scored tablets of 100 mg. Initially, give half a tablet 4 times daily with meals or milk, increasing in one week to one tablet q.i.d. Increase to two tablets q.i.d. if necessary, and reduce if possible to as low as half a tablet q.i.d. after control. Continue through acute attacks, which can be concomitantly treated with phenylbutazone.

Patients on other uricosurics may be transferred to this drug at full dosage.

Contraindications
Active peptic ulcer. Salicylates and citrates antagonize the drug's action and are contraindicated for concomitant use.

Warning
Use with caution in pregnant women.

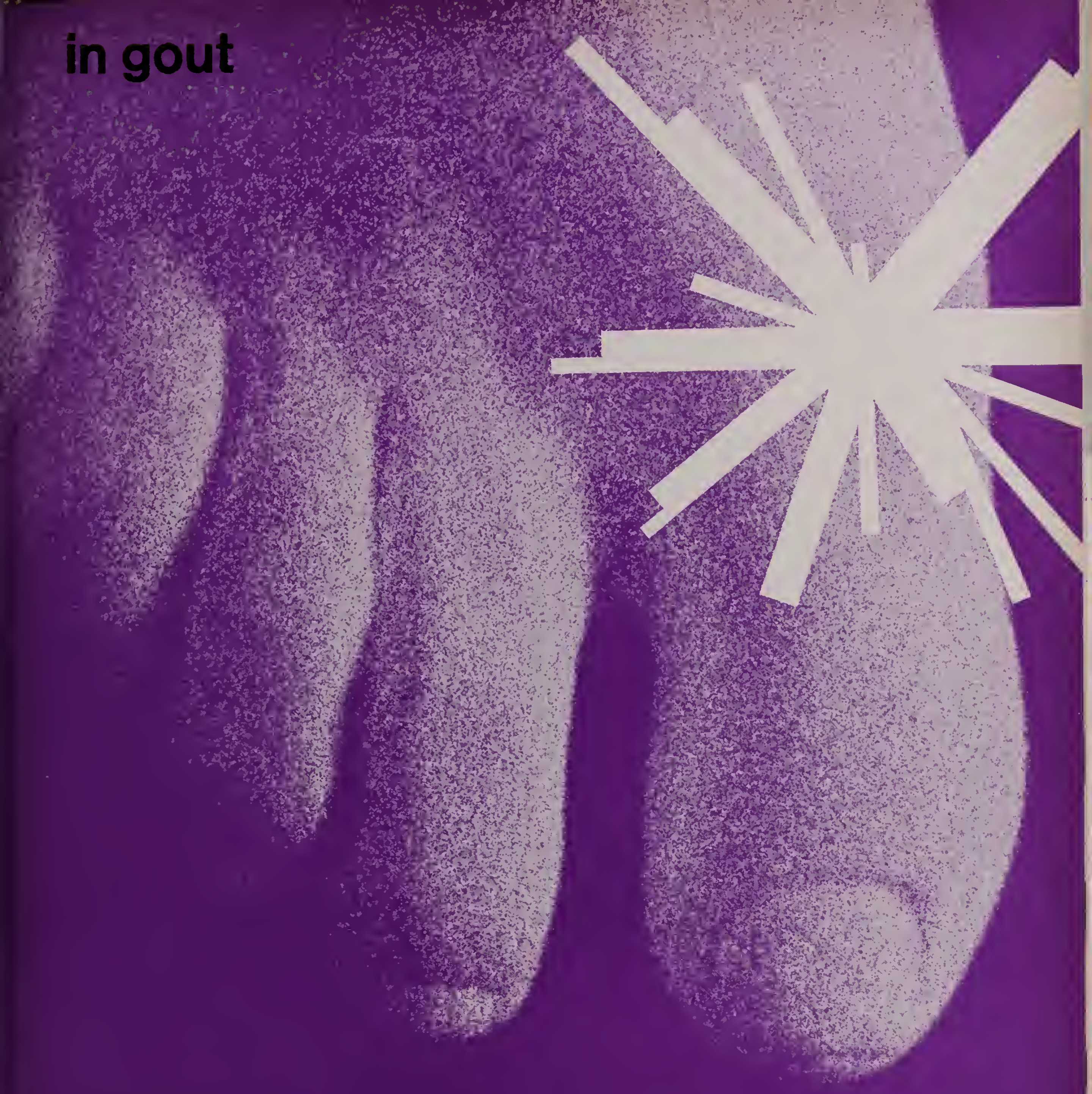
Precautions
Keep patients under close supervision and make periodic blood counts. Use cautiously in patients sensitive to pyrazoles, in patients with histories of peptic ulcer, and in conjunction with sulfa drugs, the sulfonylurea hypoglycemic agents, and insulin, the actions of which may be potentiated.

In mobilizing urate deposits, the drug may precipitate acute attacks of gout, urolithiasis, and renal colic, especially in the initial stages of therapy. Ensure adequate fluid intake and alkalinize the urine. With renal impairment, test renal function periodically.

Adverse Reactions
The most frequent are upper gastrointestinal disturbances. The drug may activate peptic ulcer. Rash occurs infrequently. Although not reported to date, blood dyscrasias are a possibility.

Geigy Pharmaceuticals
Division of
Geigy Chemical Corporation
Ardsley, New York

AN-3634PC



Anturane®
brand of sulfinpyrazone

'the most effective and best tolerated of the currently available uricosuric agents for the control of gout.'*

Geigy

Anturane, brand of sulfinpyrazone, was developed in the Geigy laboratories. Its pharmacologic activity is limited almost exclusively to increasing the urinary excretion of uric acid. For this reason, it is a drug of choice in chronic tophaceous gout and acute intermittent gout. It is not intended for relief of acute attacks of gout.

In most patients, the drug rapidly reduces serum uric acid levels to normal. This not only prevents new tophi but also mobilizes and promotes the excretion of urates already in the tissues. The reduction of tophi and periarticular crystals results in more mobile, less painful joints.

Anturane, brand of sulfinpyrazone, materially reduces the number and severity of acute attacks of gout. It may also be used to counteract hyperuricemia induced by certain diuretics.

Because of its potency, the drug is often effective in patients refractory to other uricosuric agents. Patients can usually be maintained indefinitely on it without cumulative effects or development of tolerance.

*Kuzell, W. C., et al.: Effect of sulfinpyrazone on serum uric acid in gout: a long-term study, Geriatrics 19:894, 1964.

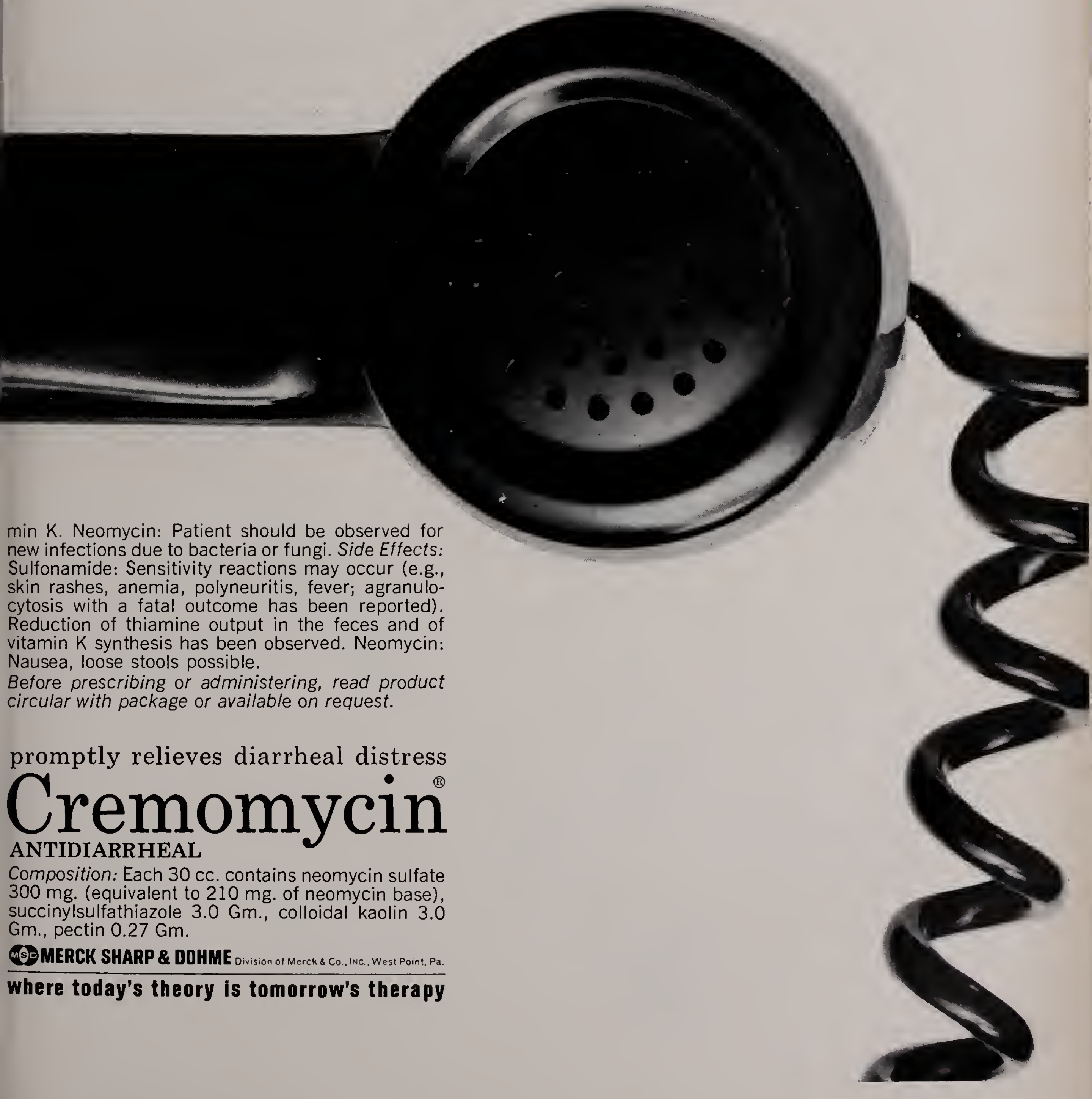
When uncontrolled diarrhea brings a call for help

When the diarrhea sufferer has run the gamut of home remedies without success, pleasant-tasting CREMOMYCIN can answer the call for help. It can be counted on to consolidate fluid stools, soothe intestinal inflammation, inhibit enteric pathogens, and detoxify putrefactive materials—usually within a few hours.

CREMOMYCIN combines the bacteriostatic agents, succinylsulfathiazole and neomycin, with the adsorbent and protective demulcents, kaolin and pectin, for comprehensive control of diarrhea.

Indications: Diarrhea. *Contraindications:* Kaolin: Withhold if diverticulosis is present or suspected. *Precautions:* Sulfonamide: Continued use requires supplementary administration of thiamine and vita-

your ℞ for Cremomycin can provide relief



min K. Neomycin: Patient should be observed for new infections due to bacteria or fungi. *Side Effects:* Sulfonamide: Sensitivity reactions may occur (e.g., skin rashes, anemia, polyneuritis, fever; agranulocytosis with a fatal outcome has been reported). Reduction of thiamine output in the feces and of vitamin K synthesis has been observed. Neomycin: Nausea, loose stools possible.

Before prescribing or administering, read product circular with package or available on request.

promptly relieves diarrheal distress

Cremomycin®

ANTIDIARRHEAL

Composition: Each 30 cc. contains neomycin sulfate 300 mg. (equivalent to 210 mg. of neomycin base), succinylsulfathiazole 3.0 Gm., colloidal kaolin 3.0 Gm., pectin 0.27 Gm.

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where today's theory is tomorrow's therapy

"...it is extremely difficult and sometimes impossible to differentiate between 'pure depression' and anxiety and it is questionable whether depression without a certain degree of anxiety really exists."

Lehmann, H. E., Canad. Psychiat. Assn. J. *4(S)*: 1-12, 1959

anxiety
depression
anxiety
depression

An antidepressant designed for the clinical realities of office practice

As many physicians have reported, the large majority of neurotic depressed patients suffer from both depression and anxiety. It may be difficult to decide whether these patients are primarily depressed or primarily anxious. And yet drug treatment of only the symptom which seems more prominent may exacerbate the untreated element of the depression complex.

Consequently, it would seem that therapy specifically aimed at both the depression and associated anxiety and tension should increase success in treatment.

This is one of the important reasons why 'Deprol' has proved particularly helpful. For 'Deprol' acts rapidly both to lift the mood and to relieve the associated anxiety, tension and insomnia.

And side effects, at recommended dosage, have been infrequent and generally readily controlled.

Indications: 'Deprol' is useful in the management of depression, both acute (reactive) and chronic. It is particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination. It is also useful for management of depression and associated anxiety accompanying or related to organic illnesses.

Contraindications: Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

Precautions: *Meprobamate*–Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

Benactyzine hydrochloride—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

Supplied: Light-pink, scored tablets, each containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.

Before prescribing, consult package circular. CD-5749

Deprol®

meprobamate 400 mg. +
benactyzine hydrochloride 1 mg.

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FREO, BY SAUNDERS SCHULTZ

FREE YOUR PATIENTS from

√ deficient neutralization

√ poor taste

√ burdensome cost

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- **effective neutralizing power**—Two tablets in vitro[1], provide nearly 2 hours' relief within effective pH range 3 to 5.5.
- **pleasant taste**—A fresh mint flavor patients continue to enjoy, because with Dicarbosil's unique* formulation, chalky aftertaste is no longer a problem.
- **exceptional economy**—Due to its high neutralization capacity combined with low cost (1¢ or less per tablet), Dicarbosil is within the reach of all patients.

1. Schleif, R.H.: J.A.PH.A., 46:179,1957 *U.S. Pat. No. 3,062,714

Active Ingredients: Calcium Carbonate Precipitated 0.489 Gm., Magnesium Carbonate 0.011 Gm., Magnesium Trisilicate 0.006 Gm.

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brand of
chlorthalidone

the longest-acting diuretic

Indications: Many types of edema involving retention of salt and water.
Contraindications: Hypersensitivity and most cases of severe renal or hepatic disease.
Warning: With administration of enteric-coated potassium supplements, the possibility of small bowel lesions should be kept in mind.
Precautions: Reduce dosage of concomitant antihypertensive agents by at least one-half. Discontinue if the BUN rises or liver dysfunction is aggravated. Electrolyte imbalance and potassium depletion may occur; take special care in cirrhosis or severe ischemic heart disease, and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended.
Side Effects: Agranulocytosis, constipation, dizziness, dysuria, headache, hyperglycemia, hyperuricemia, impotence, leukopenia, muscle cramps, nausea, postural hypotension, purpura, thrombocytopenia, transient myopia, urticaria, vomiting and weakness.
Average Dosage: One tablet (100 mg.) daily with breakfast.
Availability: Tablets of 100 mg. in bottles of 100 and 1000.
For full details, see the complete prescribing information.

*Dorhout Mees, E.J., and Geyskes, G.G.: Acta med.scandinav. 175:703,1964.

Photos: A 59-year-old woman with hypertensive cardiovascular disease and edema resistant to low-salt diet and bed rest. The patient lost 8½ lbs. in one week with a single tablet daily of Hygroton, brand of chlorthalidone.

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good riddance

Hygroton, brand of chlorthalidone, gets rid of edema efficiently. Your edematous patients will generally need far fewer tablets than with most diuretics. And they'll generally save more on prescription costs. One tablet a day is a popular dosage. So is one tablet every other day. You may even find half a tablet three times a week does the job. No other diuretic works as long. And none has as much natruretic activity per tablet.* For good riddance of edema with the least number of tablets, prescribe Hygroton, brand of chlorthalidone.

Hygroton® brand of chlorthalidone Geigy

Minnesota Medicine at a Glance

Digitalis in Pediatric Patients, Lade Page 1425

Because a large majority of infants who develop congestive heart failure die in infancy, it is extremely necessary to be able to adequately diagnose and treat these infants in the early stages. The recognition of this condition and the details necessary in the treatment are lucidly described in this manuscript.

Gardner's Syndrome, Shook and Windschitl Page 1431

Gardner's syndrome of polyposis of the colon, osteomatosis, and soft tissue tumors sometimes referred to as Peutz-Jeghers syndrome, is considered to be a familial disorder probably due to a defective gene with a dominant mode of inheritance. A soft tissue tumor in the frontal sinus and multiple polypae in the colon are illustrated in this manuscript.

Gastrostomy Tube for Infants, Root Page 1433

The use of a Davol tube for gastrostomy in infants is well worth consideration as has been described in Dr. Root's manuscript. In the infant with congenital esophageal atresia, or some other disease in which gastrostomy is urgently indicated, it is pointed out that there are some hazards associated with the continuous pressure of other types of gastrostomy tubes which, because of lack of resilience, can cause pressure necrosis in the wall of the stomach.

Pseudocysts of the Pancreas, Perry and LaFave Page 1440

A pseudocyst of the pancreas can be an annoying type of disease. There have been a variety of surgical procedures designed to eliminate the cyst. Perry and LaFave have produced the best results with the use of a cystjejunostomy Roux-en-Y procedure.

Though one does not often encounter pancreatic cysts it is well to keep in mind the variety of procedures that are used for this condition. Therefore a review of this manuscript is of value.

Sickle Cell Disease, Shook and Windschitl Page 1445

Sickle cell disease occurs only in the Negro, and whenever hematuria is encountered in these individuals, sickle cell hemoglobinopathy should be suspected.

The hematuria associated with this condition almost always stops spontaneously; there is no specific treatment. Bed rest and transfusions as indicated seem to offer the best approach to this problem.

Unilateral Pulmonary Edema, Perlman Page 1450

Treponea is a clinical condition wherein breathing is comfortable in one position but not in another. A documented case report proving the presence of pulmonary edema on one side has been recorded by Perlman. This elderly patient responded to treatment by the administration of Digoxin and Mercurhydrin.

Seizures, Gumnit Page 1453

The chief problem facing a physician is to determine the cause of seizures, as many seizures are not what is commonly known as epilepsy. There are a considerable number of causative factors which are reversible, and there are also other types of seizures which require specific therapy. Without differentiating the various types of seizures one cannot intelligently treat a patient who is suffering from these symptoms. The cryptogenic seizures which form a large part of the epilepsy pattern are ideopathic in nature, though they do have a slight tendency to appear in families.

Papillary Muscle Dysfunction, Burns and Layman Page 1458

In ventricular systole the first area of the myocardium to contract are the two papillary muscles of the left ventricle. The increased pressure within the heart tends to balloon the mitral leaflet toward the atrium, but because of the firm anchor of the contracted papillary muscles, only the diaphragm of the leaflets moves, and the free edges being held within the ventricular cavity undergo a ballooning effect so as to cause a tight closure of the mitral valve. Infarction of these papillary muscles could cause disruption of the normal architecture and consequent episodes of mitral insufficiency, as observed in the case reported by Burns and Layman.

The Acutely Injured, Root Page 1497

The greatest mortality among the acutely injured patients occurs within the first few hours following injury, and it is therefore important that the dangers of mobilization, transportation and the importance of early treatment be well understood in an effort to diminish this high mortality.

At Ancker Hospital, before an acutely injured individual is extensively moved about, he is rapidly but meticulously evaluated because the loss of blood, the hypotension, and the possibility of cord transection all may be aggravated by careless mobilization.

If respiratory insufficiency is then observed it is immediately followed by treatment through the introduction of an open airway, or if pneumothorax is evident this complication receives priority as it is the least well tolerated and must be corrected before any of the other vital signs can be attended to. Until the vital signs are stabilized the patient is maintained immobilized until his clinical status can be fully evaluated.

Herniated Disc, Neurological Conference Page 1507

The low back pain scale is on occasion one of the helpful tests designed in connection with the Minnesota Multiphasic Personality Inventory test to differentiate between organic back pain and that type of back pain which could be a conversion reaction and hypochondriasis.

Intervertebral disc compression most commonly observed in the fifth lumbar nerve or in the first sacral nerve does provide some fairly definite clinical manifestation. An evaluation of this annoying and disabling back symptom is clearly detailed in the Neurological Conference.

School Failure — Jensen Page 1515

When a child begins to fail in school a vicious cycle may develop in which he recognizes his own inability to compete successfully. He senses the disappointment in his parents; he feels the loss of acceptance by his schoolmates. With this there is a change in his general behavior and he may develop a host of physical complaints which in turn provide excuse for repeated absences from school. The attitudes of the teacher, his parents, and his doctor can either help or hinder the proper adjustment process, which must be recognized early in order that remedial measures can be instituted.

Sudden Death, Edwards Page 1519

This pathologic description of sudden death is a classic. In order to obtain an awareness of the potential problems with which the clinician may be faced when he encounters sudden death, a review of this classic manuscript would be well worth the effort.

Carbon Monoxide Intoxication, Grand Rounds Page 1537

The average motor vehicle produces in its exhaust, 3.5% carbon monoxide and 11.5% carbon dioxide. The principal mode of action of carbon monoxide in the body is by a reversible combination with circulating hemoglobin. Its lethal effect is by way of blocking out the oxygen-carrying capacity of the hemoglobin, thereby causing anoxia.

As a driving hazard, carbon monoxide produces an effect on the eyes and, in addition, weakness to the muscles of the body. A blood carbon-monoxide level of 15% would be sufficient to cause the toxic symptoms. Treatment consists in the use of hyperbaric oxygen administration, mercury-vapor light and succinic acid.

Hemolytic Anemia and Open Heart Surgery, Green Page 1545

A new syndrome of hemolytic anemia is being observed following open heart surgery. Hemoglobinemia and hemoglobinuria occur almost routinely following extracorporeal circulation. This type of hemolytic anemia falls into two categories: that in which the mechanical factor alone appears to be responsible and an autoimmune state, the pathogenesis of which is not clear.

In those instances in which a mechanical abnormality is the sole producing factor, reoperation for correction of the mechanical defect is recommended. For that type in which antiglobulin tests are positive, a response to corticosteroids has been found satisfactory.

Family Planning, Hakanson Page 1557

Ignorance, political opposition, and religious prejudice have been the major deterrents to the sensible application of contraceptive methods, but these barriers are gradually being eliminated and with this, reliable methods for family planning become possible.

Physician's Diary

I am wealthy in my friends — Shakespeare

Dr. Edward S. Judd, head of a section of surgery in the Mayo Clinic, Rochester, and professor of surgery in the Mayo Graduate School of Medicine, received a Distinguished Alumnus Award from the Geisinger Medical Center at Danville, Pennsylvania.

* * *

Dr. William C. Bernstein, Director, Division of Proctology, University of Minnesota, was elected Vice President of the American Proctologic Society, at its annual meeting in Minneapolis, June 14th.

* * *

Dr. Louis A. Brunsting, senior consultant in dermatology in the Mayo Clinic, Rochester, and professor of dermatology in the Mayo Graduate School of Medicine, University of Minnesota at Rochester, gave the Fifth Paul A. O'Leary Memorial Lecture at the annual meeting of the Minnesota Dermatological Society at Rochester in September.

* * *

Dr. A. I. Arneson of Morris was named recipient of the WCCO Radio "Good Neighbor Award" in August.

* * *

Dr. Benjamin M. Tuma of the Family Medical Clinic in Montgomery, has been elected to active membership in the American Academy of General Practice.

* * *

Dr. A. S. Zelickson of Minneapolis, assistant professor of Dermatology at the University of Minnesota, was the guest speaker in a course of dermalpathology of the Skin and Cancer Hospital of Philadelphia, held September 27th through October 1st.

* * *

Dr. William H. Remine, head of a section of surgery in the Mayo Clinic, was elected president of the Minnesota Surgical Society at the annual meeting of the group at Duluth in July, and **Dr. Edmund C. Burke**, a consultant in pediatrics in the Mayo Clinic, was elected first vice president of the Southern Minnesota Medical Association at the group's annual meeting.

* * *

NEW LOCATIONS: **Dr. F. D. Banfield** has become associated with the Olmsted Medical Group . . . **Dr. Ray Magnuson** of Cambridge has left that town for Gendeberet, Ethiopia, where he will work in a leprosarium . . . **Dr. Earl H. Wood**, Mayo Clinic, will study for a year in the Physiology Institute at the University of Berne in Switzerland . . . **Dr. J . A. Stenzel** of Minneapolis has begun practicing medicine at the new Meany and Meeking Medical Center . . . **Dr. Quentin F. Knauer** of Cleveland, Ohio, has become associated with **Drs. Jose** and **Alayne Aruguete** at the Sandstone Clinic . . . **Dr. Charles A. Tietz** has joined the Lenont-Peterson Clinic in Virginia . . . **Dr. Daniel Johnson** has joined the Litchfield Clinic . . . **Dr. Thomas G. Birkey** has joined the medical staff of the Montevideo Clinic . . . **Dr. Robert W. Schulz** opened up new offices in Fairmont, and **Dr. Robert Zemke** has joined his father, **Dr. E. E. Zemke**, in the practice of medicine in Fairmont . . . **Dr. Adrian Kapsner** has left the Hutchinson Medical Center to accept a position as resident in radiology with the Veterans hospital in Minneapolis . . . **Dr. George Miks** has joined the staff of the Ely Clinic . . . **Dr. Reginald G. Bickford**, neurophysiologist in the Mayo Clinic, has left Rochester for the Far East and Europe where he will participate in international meetings with other specialists in his field.

* * *

Dr. F. R. Kotchevar has retired from his association with the East Range Clinic at Eveleth and Virginia after thirty-seven years with that group. A testimonial dinner was given by the people of Eveleth in appreciation of **Dr. Kotchevar's** years of service to that community. Future plans of Dr. and **Mrs. Kotchevar** are indefinite at this time.

* * *

At the September 10 meeting of the Southern Minnesota Medical Association the following officers were elected: **Dr. George Stahl**, Austin, President; **Dr. Edmund Burke**, Rochester, First Vice President; **Dr. John J. Eustermann**, Mankato, Second Vice President; and **Dr. Robert H. Conley**, Mankato, Secretary-Treasurer. **Dr. Donald H. Freeman** of the Mankato Clinic received the Bronze Award for the best case report for a paper entitled "Myxedema Coma, Associated with a Suprasellar Tumor," and **Dr. Jack L. Pulec** of Rochester received the Bronze Award for the best paper entitled "Surgical Treatment of Dizziness."

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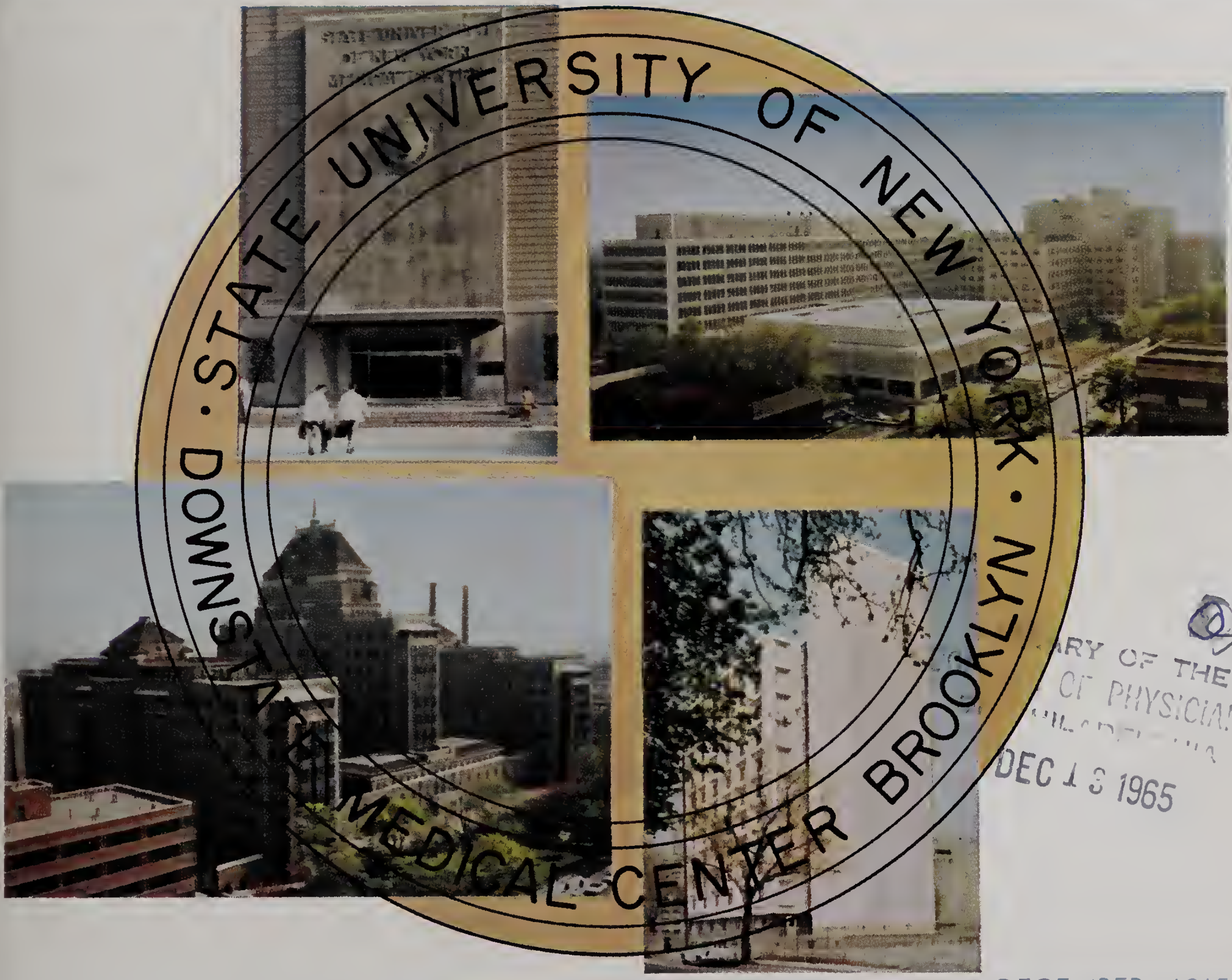
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Volume 48

Number 12

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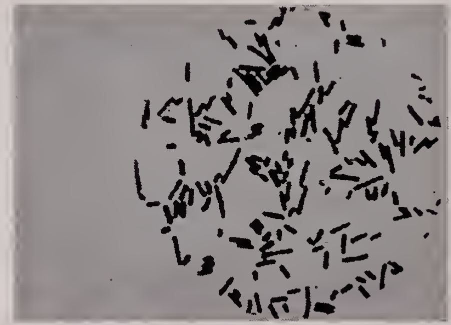

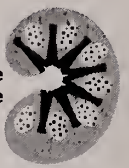

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President's Letter

This has been an eventful year for the Minnesota State Medical Association. In the future, 1965 will probably be recorded as a turning point primarily because it marked the advent of government responsibility for the medical care of a large segment of the population. It is too early to determine whether the medical profession will be able to influence the application of this new system of care so that our traditional freedoms will be reasonably maintained or whether truly socialized medicine will make its first great inroad. There are forces within our society which can be mobilized behind the ideals of medical freedom effectively enough to preserve them. Intelligent political action by the medical profession and its allies will be necessary to accomplish this since it seems evident that political action has been effective in molding the changes now upon us.

If medicine is to function with freedom under a system primarily voluntary or with comparable freedom under government sponsorship, it seems to me that the profession must be organized to demonstrate to the public that the best possible care is readily available to all. Standards of excellence must be determined and the methods of ensuring them must be strengthened. In this endeavor no factor is more important than a friendly and effective cooperation between hospitals and their medical staffs. Medicine needs spokesmen who can interpret adequately our ideals to all segments of society including those which are politically oriented.

With these thoughts I come to the end of my term of office. To all of our membership I give my thanks for the opportunity to have served, and for the cooperation of those who have labored with me in the affairs of the Minnesota State Medical Association I am grateful.

It is a pleasure to acknowledge the efforts of the editor of this journal, Dr. Carl Rice, in producing and maintaining a superior publication. In this special issue we salute the Downstate Medical Center of the State University of New York and its president and dean of the College of Medicine, Dr. Robert A. Moore. This Brooklyn institution has strong ties with Minnesota. Dr. Dennis, the chairman of the Department of Surgery, was associated with the University of Minnesota for 16 years. Several eminent members of the faculty, Dr. Millins in radiology, Drs. Karlson, Enquist, Kaplan, and Fries in surgery, received their training in Minnesota, and Downstate Medical Center has contributed a Markle Scholar, Dr. Eugene Bernstein, to Minnesota. The Downstate Medical Center is the only medical school in Brooklyn and Long Island, an area with 7,000 physicians and a population of 4½ million. Dr. Moore writes that "We hope many of our Minnesota colleagues will be encouraged by this special issue to pay us a visit." We welcome these contributions which were prepared under the supervision of Dr. Dennis.

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J. M. Stickney, M.D.
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Effects of Hypertonic Glucose

on Small Bowel Motility and Absorption

A. E. HELFT, M.D.*
C. J. BRANDWEIN, M.D.**
E. F. McNALLY, M.D.†
H. B. NEEL, A.B.‡
C. DENNIS, M.D.§
Brooklyn, New York

THE "DUMPING SYNDROME" which occurs after gastric resection consists of sweating, unpleasant warmth, subjective flushing, nausea, palpitation, and explosive diarrhea, during or within 15 minutes after eating and lasting up to 45 minutes. These symptoms are partially or completely relieved by lying down.

The most widely accepted explanation is a loss of circulating plasma volume into the intestine. This was suggested by Roberts and associates,[1] who used the observation of Lapp and Diebold[2] that the instillation of 50 per cent glucose into the jejunum can reproduce most of the signs and symptoms of the "dumping syndrome." On the other hand, Butz[3] found that during "dumping" induced in this manner the plasma volume was maintained. Amdrup and associates[4] noted that the decrease in plasma volume was less than the volume of fluid accumulating in the small intestine, while the loss from the thiocyanate (interstitial) space was approximately equal to the increase in intestinal intraluminal volume.

A second current theory for the production of the "dumping syndrome" relates the symptoms to the release of serotonin from the argentaffin cells of the duodenum and jejunum.[5-9] The thesis here is that the observed increase in intestinal activity, the explosive diarrhea, the flushing, the sense of warmth and of faintness are secondary to the action of serotonin. Increased serotonin in the portal venous blood has been observed on exposure of the small intestine to hypertonic solutions such as 50 per cent glucose.[6]

A third mechanism was suggested by Machella,[10] namely, that there is distention of the jejunum and duodenum caused by the introduction of hypertonic materials into the small intestine. Machella was able to produce

---

*Assistant Instructor, Department of Surgery.
**Fellow in Gastroenterology, Department of Medicine.
†Instructor, Department of Medicine.
‡Fourth year medical student from Albert Lea, Minnesota.
§Professor and Chairman, Department of Surgery.

From the Departments of Medicine and Surgery, State University of New York, Downstate Medical Center, Brooklyn, New York.

Supported by grant #AM09546-01 from the National Institute of Health, The State University of New York, The Gelb-Strauss Fund for Medical Research, and the Southern New York Medical Education and Research Foundation.

most of the symptoms of "dumping" by blowing up a balloon in this segment of the intestine.

It appears to the authors that these explanations and the several now discarded theories of the origin of the "dumping syndrome" singly or in conjunction fail to explain the symptoms observed. Because hypertonicity appears to be the common denominator in all of the prevailing theories of the cause of the "dumping syndrome," we have studied the effect of intraluminal placement of hypertonic solutions on intestinal absorption and motility in the conscious dog.

Procedure

To study absorption under circumstances in which the small bowel does osmotic work, a 40-cm. ileac Thiry-Vella loop[11] was prepared, in which both ends of the segment isolated from the main intestinal stream were brought out through the left flank. Twenty-five ml. of a solution half-isotonic in NaCl and half-isotonic in Na_2SO_4 was introduced over a 60-second period into the loop at body temperature, and the ends were closed with conical stoppers. Samples of 0.2 ml. were drawn every 10 minutes over the next hour, and the chloride concentration in the specimens was measured with a Buchler Cotlove Chloridometer. Following the control determinations, the loop was bathed with 25 ml. of 50 per cent glucose (37° C) in water for five minutes. The segment was then gently flushed out with chloride-sulfate test solution, and 25 ml. of test solution was instilled into the lumen as in the control observation. Specimens of 0.2 ml. volume were removed every 10 minutes for one hour and analyzed for chloride content.

Motility patterns of the main stream of the small bowel were recorded through open-tipped water-filled polyvinyl catheters of 1.4 mm. internal diameter. The catheters were introduced into a jejuno-cutaneous Roux-Y preparation,[12] and intraluminal pressure changes were detected with a strain gauge and recorded on a Sanborn multichannel recorder.

All animals were studied in the fasting state without the use of anesthetics or narcotics and with the animal lying on his right side.

Results

The Effect of a Hypertonic Solution on the Absorption of Chloride from an Ileac Thiry-Vella Loop

When 25 ml. of a solution which is half isotonic in NaCl and half isotonic in Na_2SO_4 is placed within the Thiry-Vella loop, more than 90 per cent of the fluid is absorbed from the loop within 60 minutes, and the chloride concentration falls from 71 mEq/L to 10 mEq/L (Figure 1). Data from 12 experiments show a 50 per cent average drop in chloride concentration in 20 minutes.

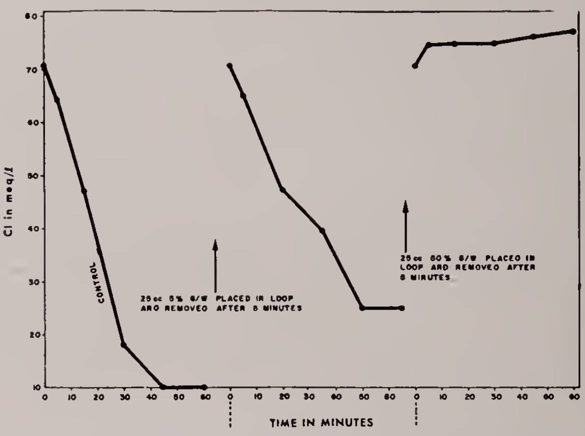

Fig. 1 — When 25 ml. of a test solution half-isotonic in NaCl and half-isotonic in Na_2SO_4, which contains 78 mEq/L of chloride ion, is placed in a Thiry-Vella loop, the chloride concentration in the loop drops to 10 mEq/L over the 60-minute test period. This is the control state. After the loop is washed with 5 per cent glucose in water for five minutes, a similar pattern of chloride absorption is obtained. However, when the loop is washed for five minutes with 50 per cent glucose in water, there is no chloride absorbed over the test period of one hour.

When the loop is washed with 25 ml. of 5 per cent glucose in water (37° C) for five minutes and the NaCl-Na_2SO_4 solution then instilled, a similar pattern of chloride absorption is obtained.

On the other hand, when the loop is washed with 25 ml. of 50 per cent glucose in water (37° C) for five minutes, there is no appreciable absorption of fluid or chloride ion from the subsequently instilled NaCl-Na_2SO_4 solution over the test period of one hour.

In three experiments, control observations of chloride absorption from the test solution were followed by multiple observations of chloride absorption after a single five-minute period of flushing with 50 per cent glucose solution. All remaining fluid was flushed out of the segment with test solution every 20 minutes over a two and a half hour period, and chloride concentration was followed through each 20-minute interval. There was return of some selective absorption of chloride ion only after one and a half hours following the 50 per cent glucose wash. At 100 minutes after the 50 per cent glucose instillation, the ileum reduced the intraluminal chloride concentration from 80 mEq/L to 66 mEq/L in 20 minutes, as compared to the control of 80 mEq/L to 38 mEq/L in 20 minutes. Return to control performance did not occur in two and a half hours (Figure 2).

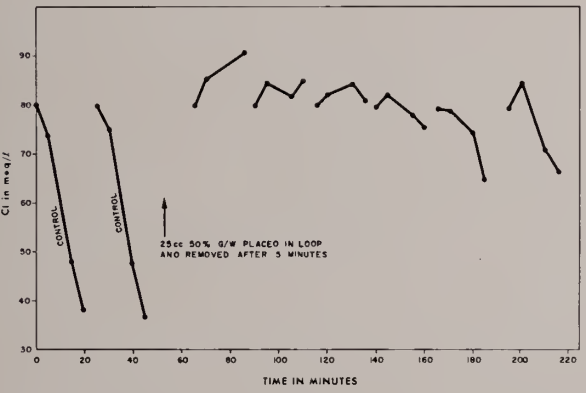

Fig. 2 — When 25 ml. of a test solution half-isotonic in NaCl and half-isotonic in Na_2SO_4, which contains 78 mEq/L of chloride ion, is placed in a Thiry-Vella loop, the chloride concentration in the loop drops to less than 40 mEq/L in 20 minutes. After the loop has been washed with 50 per cent glucose in water for five minutes, chloride absorption from the test solution is impaired. New test solution was placed in the loop every 20 minutes, and only after 120 minutes following the 50 per cent glucose in water does the absorption of chloride ion from the test solution begin to return to control rates.

Chloride absorption was also studied repeatedly in a dog which had both a Thiry-Vella loop and a jejuno-cutaneous Roux-Y anastomosis. When 50 per cent glucose in water was instilled into the bowel through the Roux-Y anastomosis, and chloride absorption from the instilled NaCl-Na_2SO_4 solution was measured simultaneously in the Thiry-Vella loop, a normal pattern of chloride absorption was obtained.

The Effect of Hypertonic Solutions on Jejunal Motility

A triple-lumen catheter with openings 5 cm. apart was introduced into a jejuno-cutaneous Roux-Y preparation, and a record of jejunal pressure patterns as shown in Figure 3 was obtained. After a period of control observation, 50 ml. of 50 per cent glucose in water at 37° C was instilled at a rate of 10 ml./minute into the bowel at a point 5 cm. distal to the recording catheters. Within five minutes of the instillation of the hypertonic solution there was a cessation of activity without a bout of initial hyperactivity. In each of 13 trials, this cessation of activity began from zero to eight minutes after the beginning of injection of 50 per cent glucose in water and persisted for periods of 35 to 215 minutes, at which time the motility gradually returned to control levels. This period of induced inactivity of the bowel was usually associated with the animal becoming drowsy. In only two of nine trials was any cessation of intestinal motility produced following the instillation of 50 ml. of 0.9-per cent NaCl into the Roux-Y fistula. Motility was abolished for 60 minutes in one and for 89 in the other.

Discussion

This study demonstrates that 50 per cent glucose abolishes the ability of the ileac mucosa to absorb chloride against an osmotic gradient as well as to absorb water. This performance of osmotic work is inhibited for periods of up to two and a half hours following the exposure of the ileac mucosa to 50 per cent glucose. Following this period, the absorption rate of chloride returns towards normal.

This action of 50 per cent glucose appears to be local. The absorption of chloride from the ileac Thiry-Vella loop was not impaired when 50 per cent glucose was instilled simultaneously into the jejunal Roux-Y fistula.

The course of the chloride concentration in the ileum in the presence of sulfate ion has been well documented in a series of excellent studies by Ingraham and Visscher.[13]

Confirmation in the Chronic Thiry-Vella loop preparation in the dog was obtained by Dennis and Visscher.[14] The possibility that gastric content or 50 per cent glucose solution might interfere with performance of osmotic work by the intestinal mucosa was suggested by the prior demonstration by one of us[15] that pure water has such an effect upon the jejunal and ileac mucosae. It is this observation that suggests that the effects of 50 per cent glucose here reported may be osmotic in mechanism rather than due to the chemical nature of glucose. Hendrix et al.[16] have demonstrated that intravenous infusion of serotonin is followed by a brief period of hyperactivity of the bowel before cessation of all activity and decrease in tone.

Summary

The effect of 50 per cent glucose on chloride absorption against an osmotic gradient has been measured in the trained, conscious dog, using a chronic Thiry-Vella loop of ileum. Fifty-per cent glucose in water inhibited the ability of the ileac mucosa to perform osmotic work as measured by absorption of chloride against a concentration gradient; 50 per cent glucose was also found to inhibit jejunal motility following instillation into a chronic Roux-Y jejuno-cutaneous preparation in the unanesthetized dog.

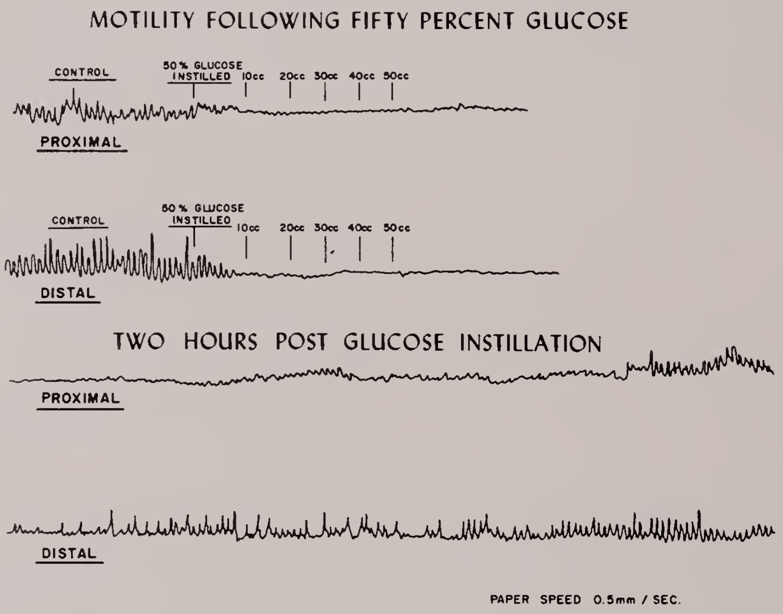

Fig. 3 — The control recording of jejunal pressure patterns consists of regular rhythmic contractions. The recording catheters are in the jejunum with the ends 5 cm. apart. Following the instillation of 50 ml. of 50 per cent glucose in water into the bowel at a rate of 10 ml./min., there is an almost immediate cessation of activity. Only after two hours does the motility return to control levels.

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Whoever undertakes to set himself up as judge in the field of Truth and Knowledge is shipwrecked by the laughter of the gods. — Albert Einstein

Pigskin Heterografts*

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ALTHOUGH THE need is admittedly small, whenever the demand for a temporary biological dressing arises, despite the urgency it is often difficult to obtain an adequate supply of suitable tissues, whether from living donors, cadavers, or tissue banks. This need for human-skin substitutes for burn victims prompted many early investigators to search for materials from animal sources. All of the efforts were doomed to failure, however, since the goal envisioned was either complete repair or permanent survival of the heterografts.

Recently, however, several investigators have suggested that heterologous tissues be used as temporary dressings for large skin defects. In 1951, Silvetti[1] proposed that a major study be undertaken to determine the practicality of using bovine embryo skin as a temporary form of biological dressing for large skin wounds, based on preliminary results from mice, rats and rabbits. In 1955, Silvetti and Menendez[1] described the use of calf-embryo skin in a 72-year-old housewife, with the graft being retained for more than two weeks. More recently, Silvetti and co-workers[1] reported that grafts of such skin persisted for eight to 16 days in mice, rats, rabbits and dogs, and left clean, smoothly granulating wounds after being sloughed. Second set grafts were retained for nine to 10 days. In addition, microscopic examination of the grafted areas showed less round cell infiltration about the bovine graft than in control homografts. Rogers and co-workers[2,3] have utilized fetal calf in humans and observed a surprising lack of host reaction to the grafts, even after 12 to 17 days of graft retention. Sokolic[4] and co-workers, however, evaluated the use of bovine embryo grafts in dogs and humans and reported that the grafts elicited a violent polymorphonuclear reaction at the graft host interface and were not effective more than four to five days.

Snyderman and co-workers[5] studied the survival of homografts and pigskin heterografts in patients with neoplastic disease and observed that pigskin was retained for more than seven days in nine out of ten patients, with two cases of prolonged survival. One patient died with the heterograft‡ still intact after 33 days; the second patient retained the heterograft for 68 days. At the same time, no antibodies against pigskin could be demonstrated in the serum of six of these patients. Eastwood[6] has also investigated the use of pigskin and found that freeze-dried pigskin remained firmly adherent and provided effective coverage for wounds in rats for an average of 14 days as compared with 21 days for freeze-dried homografts. Fresh pigskin which had been sterilized with betapropiolactone was effective for approximately 10 days. Two clinical cases were reported in this study.

Other materials which have been suggested as suitable for temporary dressings are amniotic membrane, reconstituted collagen, and open-celled polyvinyl-alcohol-formalized and polyurethrane foams. Amniotic membrane, however, does not provide the effective coverage of other materials; generally speaking, rejection times are shorter than in skin, and the thickness of the material (.2 mm–.5 mm.) prevents its use in weight-bearing areas. The narrow connective tissue zone at the graft donor interface, as would be anticipated, shows a robust inflammatory response by the seventh day. Bovine collagen is effective experimentally for approximately 14 days; however, the application of either the film or the sponge has been entirely unsatisfactory clinically as a temporary dressing in burns, and maceration and disintegration seem to be inevitable consequences. The sponges do not sufficiently adhere to the wound surfaces, and fluid collections are frequent at the wound interface. Furthermore, rigidity develops on drying, preventing its use at crease areas, and fragmentation of the protheses has occurred, with migration into the tissues.

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‡See Test Your Word Score Page 1639.

Method of Study

The urgent need for physiological skin-wound dressing material which could not be met by homografts alone, and the encouraging results of previous investigators stimulated the search for additional skin substitutes. Abundantly available, heterogenous skin was employed in the animal laboratory, using White Yorkshire pigskin and bovine collagen as graft sources. White Yorkshire pigs were selected as donors because:

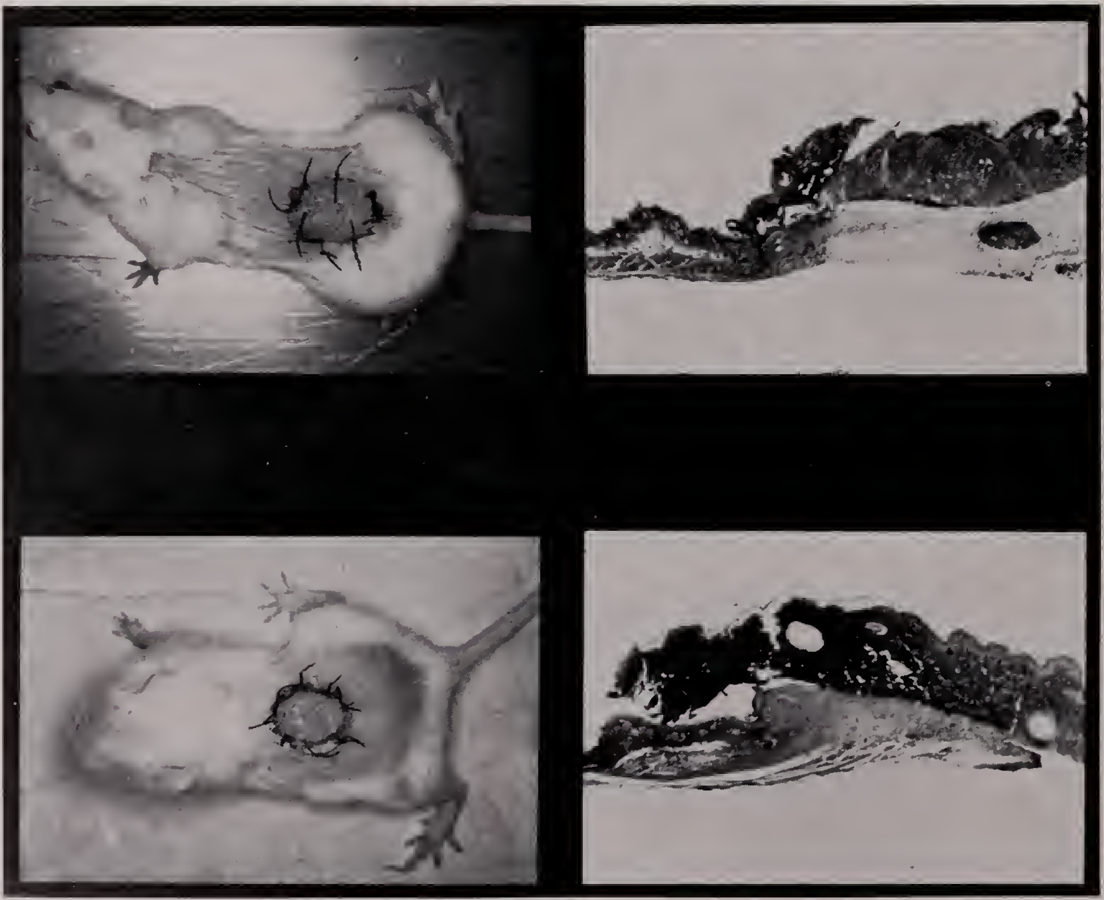

Fig. 1 — *Upper Left:* Pig heterograft on mouse at six days. Graft is soft, pink and viable. *Upper right:* Masson-stained section of six-day heterograft showing good structural integrity and little cellular infiltration. *Below left:* Pig heterograft in situ for 14 days. Essentially the same as six days except for a slightly increased dehydrated necrotic peripheral rim. *Lower right:* 14-day biopsy showing a progression of the necrotic edge; however, the structures are intact and there is little cellular infiltration.

1. Pigskin has close structural similarity to human skin.
2. There is a sparsity of hair as compared to the skin of other animals.
3. There is a readily available unlimited supply.
4. There is technical ease in obtaining split-thickness skin from the wide and tense body surface.
5. Repeated crops of skin in a short period of time are available due to the rapid re-epithelialization of skin.

Over 800 laboratory animals have been employed in varying studies to date, and 24 patients have received one or more applications of pigskin.

Results

In all of the studies, and in the patients selected, the lack of host reaction to the pigskin has been most impressive.

Table 1 is a resume of the results in homografting and in pigskin heterografting in C57 and A Heston mice (Fig. 1). It is interesting to note the retention of the pigskin heterografts for an average of 18 days as against an average of nine days for the homografts. In all of these studies the primary interest was to gain information as to the eventual use of pigskin as a temporary biological dressing, not to seek prolonged survival of pig heterografts. Irradiation of the pigskin in vitro did not materially alter our results, and second set pigskin grafts did not show accelerated responses. Vascularity studies employing Evans blue, India ink and polyvinal-pyrollidone labelled with I^{131} failed to reveal any evidence of vasculariza-

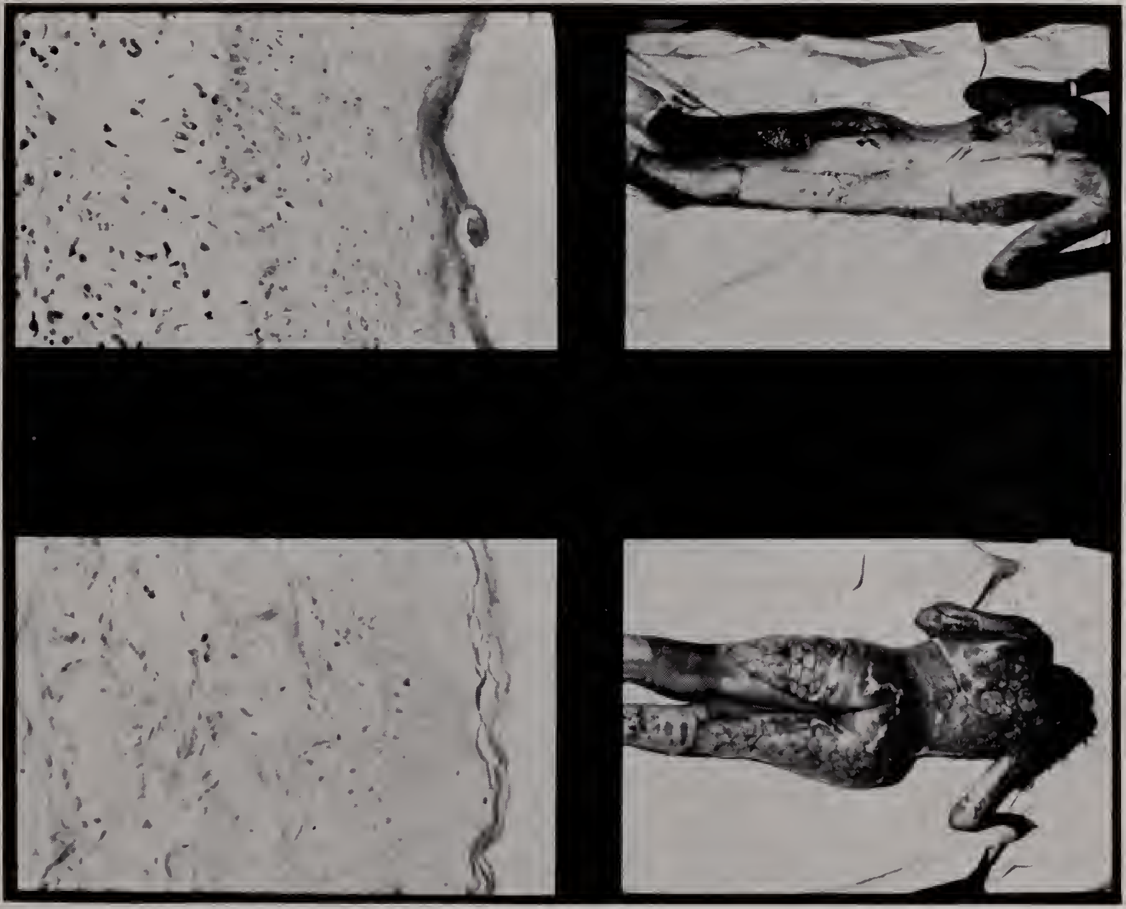

Fig. 2 — *Upper left:* Pigskin grafts five days after application to a 51% third degree burn. The grafts have good adherence, appear viable and provide effective coverage. *Lower left:* Section of the pigskin graft at eight days showing intact dermis and epidermis with little or no cellularity. *Lower right:* Normal skin with the human dermis staining a lighter green in the Masson preparation. Upper right: Patient seven months after burning and subsequent auto grafting.

tion of the pig heterografts in any of the animals examined. Freeze-dried pig grafts were also successfully retained when employed for temporary coverage. Massive grafts applied to huge wounds were remarkably satisfactory and life-saving in mice as compared to ungrafted controls, all of which succumbed within 40 hours.

Table 2 is a compilation of the results when split-skin pig grafts were applied to New Zealand white rabbits. Again longer retention was obtained with these heterografts as compared to split-skin rabbit homografts. Longer retention was also obtained in the pig grafts when animals were simultaneously homo and heterografted.

Table 3 summarizes our experience with pigskin as a temporary skin substitute in 19 patients, 14 of whom were seriously burned, although at this time an additional five patients have been heterografted (Fig. 2). None of the grafts were sutured and repeated applications were made in nine patients. In most instances the grafts have been retained for an average of two weeks. As in the use of any type of temporary covering agent, the degree of adherence and length of retention are to a large degree dependent upon the status of the wound surface upon which the grafts are applied. Whenever purulent accumulations were observed under the heterografts, the involved grafts were removed. No detrimental effects have been observed in these cases to date, although the data accumulated so far is incomplete, particularly in the immunological and bacteriological aspects.

MEAN SURVIVAL OF SKIN GRAFTS

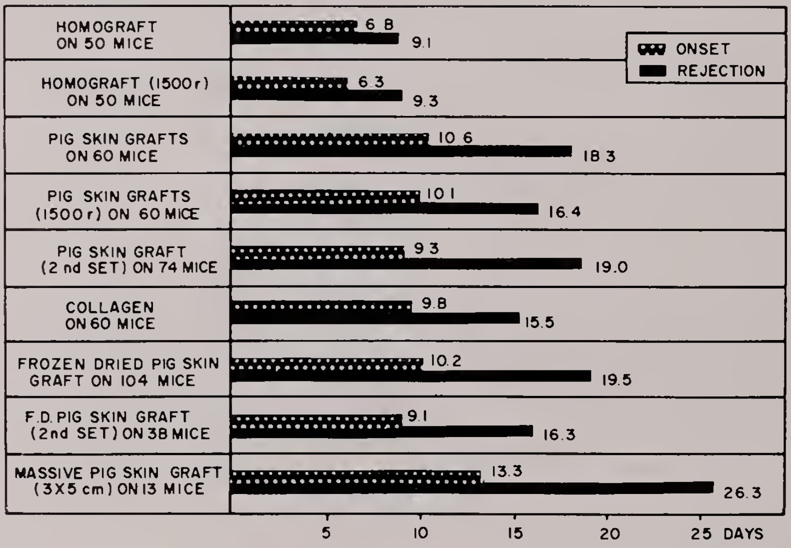

TABLE 1

MEAN SURVIVAL OF SKIN GRAFTS

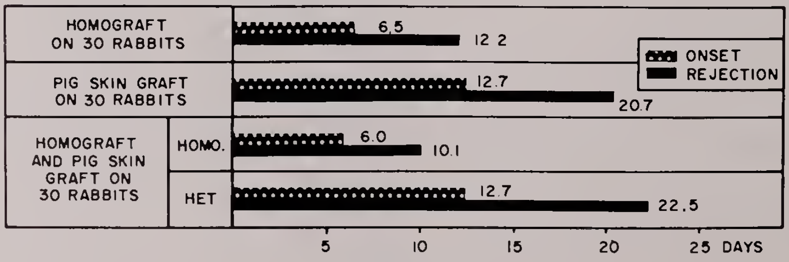

TABLE 2

Summary

An ideal temporary dressing should develop firm adherence to the wound surface, thus preventing protein and electrolyte loss, decreasing pain, and inhibiting the fibroplastic response. In addition, it should reduce bacterial growth, permit less painful dressing changes, and improve the patient's general well being. The application of biological materials over joint surfaces may even permit painless motion and conceivably reduce the degree of contractures. There can be no doubt that the judicious use of homografts in severe burns, regardless of the source, method of preservation, or state of viability, and also despite some obvious disadvantages, has proven its clinical usefulness. On the other hand, pigskin heterografts appear to offer several advantages. They remain viable in the neighborhood of two weeks and provide effective wound coverage. Repeated applications can be made without any noticeably adverse local or systemic responses, and without the slough accompanying the homograft rejection mechanism. In most instances, the application of heterografts, as in other temporary biological dressings, exerts a beneficial influence upon the wound surface, both from the standpoint of a reduced bacteriological population and a stimulating effect upon the marginal epithelium. Although pigskin has provided as effective wound coverage as other more commonly employed temporary biological dressings, it would appear at this time that it should be reserved for urgent situations where homografts are not available.

RETENTION OF PIGSKIN HETEROGRAFTS

PATIENT	SEX	AGE	DIAGNOSIS	GRAFT RETENTION	OUTCOME AND REMARKS
E.P.	F	21	2°.3° Flame Burn(53%)	4 Wks	2 Homografting.Resurfaced:Living
J.R.	M	7	3° Flame Burn(45%)	10 Days	1 Homografting:Resurfaced:Living
B.M.	M	23	3° Flame Burn(45%)	3 Wks	Resurfaced:Living
B.N.	M	29	2°.3° Flame Burn(55%)	17 Days	Resurfaced:Living
L.O.	F	10	3° Flame Burn(51%)	22 Days*.11 Days**	Pseudomonas Septicemia:Resurfaced:Living
C.M.	F	10	3° Flame Burn((40%)	16 Days	Resurfaced:Liviving
G.D.	F	24	2°.3° Burn(60%)	21 Days*.2 Days(I)**	1 Homografting:Pseudomonas Septicemia:Resurfaced:Living
M.C.	M	13	3° Burn(40%)	13 Days	Resurfaced:Living
R.W.	M	6	3° Burn(35%)	12 Days	Resurfaced:Living
F.D.	M	67	3° Burn(15%)	10 Days	10 Day Old Graft:Died of Congestive Failure·
E.M.	F	82	3° Flame Burn(20%)	1 Wk(I)	Resurfaced:Living
M.G.	F	42	3° Burn(25%)	12 Days	Resurfaced:Living
K.H.	F	4½	2°.3° Burn(40%)	14 Days*.10 Days**	Resurfaced:Living
L.M.	F	20	3° Flame Burns(85%)	3 Days	Partial Excision of Eschar:Died with Intact Heterograft
W.B.	F	3 Days	Congenital Skin Defect(9%)	109 Days	Died from Cardiac Failure with Heterograft
J.D.	M	6 Mos	Infusion Slough of Scalp	42 D.*.1 Wk**.1 Wk(I)***	Septicemia(staph.):Skull Exposed:Resurfaced:Living
C.D.	M	1 Mo	Infusion Slough of Leg	9 Days	Exposed Tibia:Resurfaced:Living
G.G.	F	70	Stasis Ulcers of Legs	4 Wks*.3Days(I)**	Resurfaced:Living
L.T.	F	81	Arteriosclerotic Ulcers	5 Wks*.3 Days(I)**	Resurfaced:Living

* 1st. SET ** 2nd. SET *** 3rd. SET (I) INFECTION

TABLE 3

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Easy Street

Easy street is always a dead-end street or a blind alley — Herbert Prochnow

Cerebral Gigantism

In 1964, Sotos, Dodge, Muirhead, Crawford and Talbot[1] reported five cases of gigantism characterized by mental retardation, clumsiness, hypertelorism, anti-Mongolian slant of the eyes and a high arched palate.

These authors discussed their cases in the light of a possible hypothalamic lesion, relating the growth disturbance to some impairment of growth-hormone release or nutritional processes.

For the past four years, the author has followed a patient of remarkable similarity except for two features: a persistent elevation of the urinary excretion of 17-ketosteroids and hydroxysteroids and an anatomical urinary tract abnormality.

The case is of interest because although it appears almost identical to the previously described group, there is demonstrable abnormal adrenal function. Here it is again attractive to postulate a hypothalamic lesion, but in this case it would appear that major emphasis should be given to those factors that control adrenocorticotropin release. The gigantism seen here may be more related to adrenal androgens than to excessive growth-hormone release and/or nutrition.

Case Report

A 3½-year-old white boy (Figure 1) was first admitted to Kings County Hospital on February 25, 1961, because of a febrile convulsion. There had been a previous episode at age 8 months. He was the product of a full-term pregnancy (complicated by pre-eclampsia), with a birth weight of 11 pounds, 9 ounces. Delivery was by cesarean section because of "increased intracranial pressure." Developmental history revealed that the patient sat at 8 months of age, stood at 13 months and talked at 2½ years. At the time of admission, he was not yet toilet-trained and was considered by his parents to be somewhat retarded when compared to his siblings. The patient's mother was not diabetic, although her mother was.

The father's height is 5 feet, 11 inches, the mother's 5 feet, 4 inches, a 19-year-old brother's 6 feet, a 14-year-old brother's 5 feet, 10 inches, and a 12-year-old sister's 5 feet, 4 inches. The tallest relative is the maternal grandfather whose height is 6 feet, 4 inches.

Physical Findings

The physical examination revealed a large, awkward child, 48 inches tall (50th percentile for 7 years), weighing 57 pounds (50th percentile for 7 years). His head circumference was 21.5 inches (50th percentile for 13 years). The ratio of the upper to lower segment was 1.3 (normal for age). His head was remarkable in that the shape was dolichocephalic (Figure 2), with hypertelorism and an anti-Mongolian slant to the eyes (Figure 3). The palate was high arched and the teeth carious. Hyperemia of the pharynx was present. There was no palpable splanchnomegaly. At this time, the genitalia were considered to be of normal size for the patient's age.

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Abnormal Urinary Corticoid Excretion

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Laboratory Findings

A spinal fluid examination revealed no abnormalities. Admission blood count and urine analysis were normal except for leucocytosis and acetonuria. The BUN was 9 mg%. Serum CO_2 was 13.4 mEq/L, Cl 103 mEq/L, Na 135 mEq/L, K 4.7 mEq/L. The following results were obtained with an oral glucose tolerance test: (1) fasting level — 91 mg%, (2) 30 minutes — 119 mg%, (3) 1 hour — 119 mg%, (4) 2 hours — 119 mg%, (5) 3 hours 109 mg%. An insulin sensitivity test gave the following results: (1) fasting glucose level — 119 mg%, (2) 15 minutes — 86 mg%, (3) 30 minutes — 70 mg%, (4) 45 minutes — 90 mg%, (5) 60 minutes — 61 mg%, (6) 90 minutes — 50 mg%. The 24-hour urinary excretion of 17-ketosteroids was 4.0 mg. and of 17-hydroxycorticosteroids 6.5 mg. There were no detectable gonadotropins in the urine. Skeletal maturation was estimated as falling within 2 standard deviations of the mean, although approaching the 95th percentile. On the skull film the measured area of the sella turcica fell within 2 standard deviations of the mean, also approaching the 95th percentile. The electroencephalogram showed a diffuse abnormality compatible with a convulsive disorder.

In June 1961, pneumoencephalography was performed. The x-ray report was as follows: "Enlarged calvarium with a proportionate ventricular system. No inordinate amount of gas is seen within the subarachnoid space, so that the above described findings are indicative of a macrocephaly."

Progress

There were two subsequent admissions for evaluation of clumsiness and for recurrent convulsions.

At age 4 and 7/12 years, a repeat bone age was equivalent to that of an 8-year-old male, this being greater than 3 standard deviations above the mean. At this same time urinary 17-ketosteroid excretion was 12.3 mg. per 24 hours.

At about the age of 6 and 11/12 years a diagnosis of urinary tract infection was made by the patient's private physician. The child was then readmitted to the hospital for evaluation of this

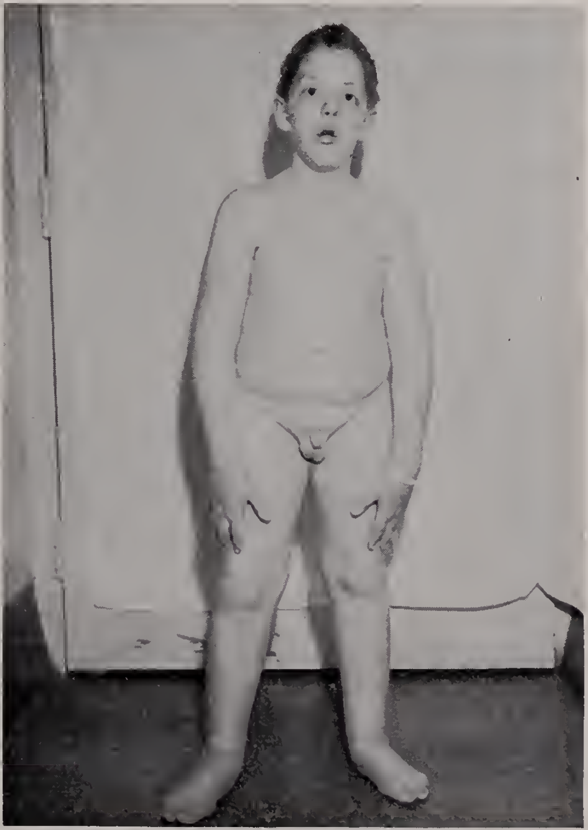

Fig. 1 — Seven and 4/12 year-old male.

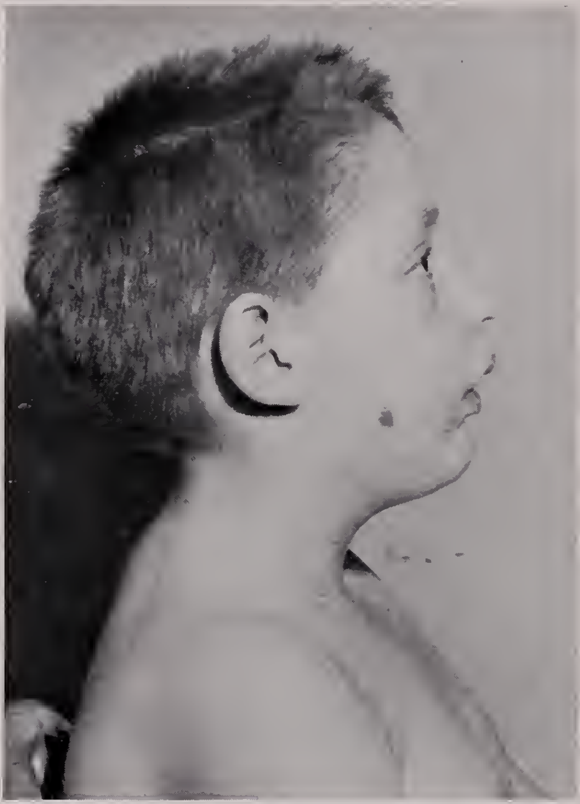

Fig. 2 — Head is dolichocephalic.

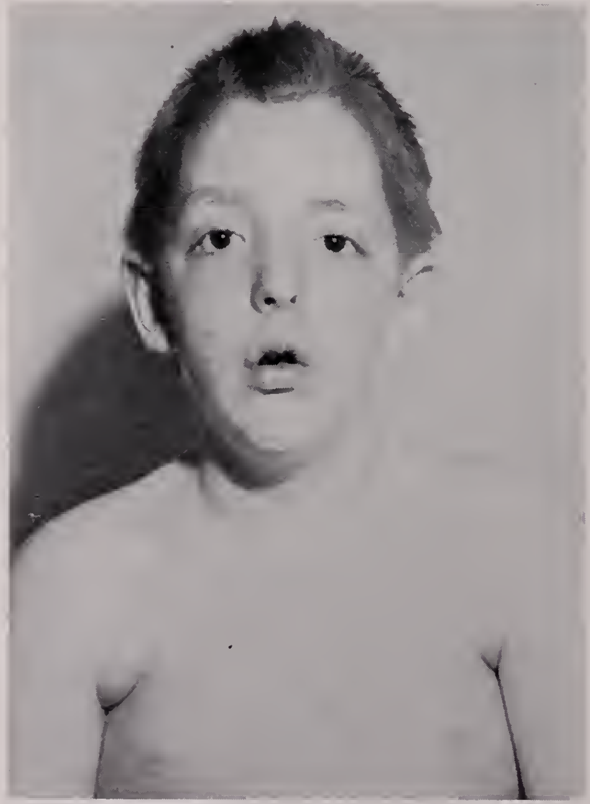

Fig. 3 — Eyes are widely spaced and show an anti-Mongolian slant.

problem. At this time the physical examination was unchanged, except that his height was 53 inches (mean for 10-year-old male), his weight 125 lbs. (50th percentile for 15½-year-old male), and his head circumference 23 inches (greater than 50th percentile for 13-year-old male). His genitalia appeared somewhat large for a prepubescent male. There was no pubic or axillary hair present.

Admission urine analysis was negative except for the presence of many white blood cells. BUN was 11 mg%. A cystogram showed the presence of "megacystis" and "megaureter" of unknown etiology, associated with an impaired ability to empty his bladder. (Bladder training was said to have been achieved by 5 years of age.) Creatinine clearance at this time was about 45% of the expected normal.

Twenty-four-hour urinary corticoid excretion remained high. The unstimulated values for 17-ketosteroids and 17-hydroxycorticosteroids were both 10 mg. Repeat serum electrolytes, glucose tolerance and insulin sensitivity curves were not significantly different from the studies performed 4 years earlier.

Baseline plasma 17-hydroxycorticosteroids were elevated on 2 occasions (32 and 29 ug% — upper limit of normal adults, 25 ug%). There was a normal response to intravenous ACTH stimulation (plasma hydroxycorticosteroids rose from 32 to 71 ug%). On the other hand there was no response to oral metapirone. The PBI was 4.4 ug%. Bone age was equivalent to that of a 10½-year-old child, representing 3 standard deviations above the mean. Both repeat films of the skull and another pneumoencephalogram were unchanged from the previous studies.

His I.Q. on the Stanford-Binet scale was 79.

Discussion

When the case was first seen, an attempt was made to determine the cause of the gigantism. Conditions recognized as being associated with accelerated growth, such as thyrotoxicosis, Marfan's syndrome, gigantism associated with lipodystrophy as described by Seip[2] could be ruled out on the basis of inspection. Adrenal disorder was not considered at this time, because the 17-hydroxysteroids did not seem remarkably elevated when interpreted in the light of the patient's large size, and the elevated 17-ketosteroids were not thought to be high enough to suggest the adrenogenital syndrome (especially in the absence of genital enlargement at that time). The investigation was, therefore, directed at ruling out pituitary gigantism associated with excessive growth-hormone secretion.

The presence of a markedly advanced bone age made this diagnosis unlikely.[3] The presence, also, of a large abnormal head and mental retardation made one consider that these features might be part of a symptom complex.

Additional factors which seemed to rule out gigantism associated with excessive growth hormone production included: (1) no demonstrable enlargement of the sella turcica, (2) excessive size at birth, (3) absent visceromegaly, (4) normal serum P, (5) a flat glucose tolerance test, (6) increased sensitivity to insulin. Not only do the two latter findings argue against excessive growth-hormone secretion, but they suggest that its secretion may be impaired. There is experimental data to support this theory. In 1948, Kinsell et al.[4] demonstrated that the treatment of acromegalics with androgens would cause a fall in serum growth-hormone levels. More recently, Frantz and Rabkin[5] have shown that treatment of patients with corticosteroids impairs the ability to secrete growth hormone.

The discharge diagnosis after the first admission was "gigantism of undetermined etiology."

The similarity between Sotos' cases and the present one is striking. The author's case shares with all or most of the five previously reported the following features: (1) mental retardation, (2) clumsiness, (3) hypertelorism,* (4) anti-Mongolian slant of the eyes, (5) high arched palate, (6) convulsive disorder, (7) abnormally large dolichocephalic head, (8) precocious sexual maturation, (9) normal sella turcica, (10) advanced bone age, (11) abnormal pneumoencephalogram, (12) maximal growth spurt ending at about four years of age (Figure 4), (13) undetectable urinary gonadotropins, (14) abnormally heavy birth weight, (15) negative family history for gigantism, (16) no laboratory findings compatible with excessive secretion of growth hormone.

The present case is unique in two features: (1) the presence of an associated urinary tract abnormality, and (2) marked elevation of the excretion of both 17-ketosteroids and 17-hydroxycorticosteroids. The first feature is considered to be a coincidental finding, unrelated to the growth problem; but the second is thought to be a variant of cerebral gigantism.

Sotos and his co-workers postulated that a hypothalamic lesion could lead to an alteration in the regulation of nutrition and/or growth-hormone release, thereby offering an explanation for the gigantism seen in their case. It should be added that Sotos et al. did not report 17-hydroxycorticosteroid values in any of their cases, nor 17-ketosteroids in two. Therefore, it cannot be stated that all of their cases lacked any disturbance in adrenal function.

The present author would also like to suggest a hypothalamic lesion in this case, but to postulate that excessive growth is related to an abnormality of the hypothalamic (hypophyseal) adrenal axis rather than to excessive growth-hormone release.

Reichlin[6] has shown that in rats the site of hypothalamic lesions which cause disturbance in growth is close to, if not identical with, the site which causes disturbances in adrenocorticotrophic hormone release.

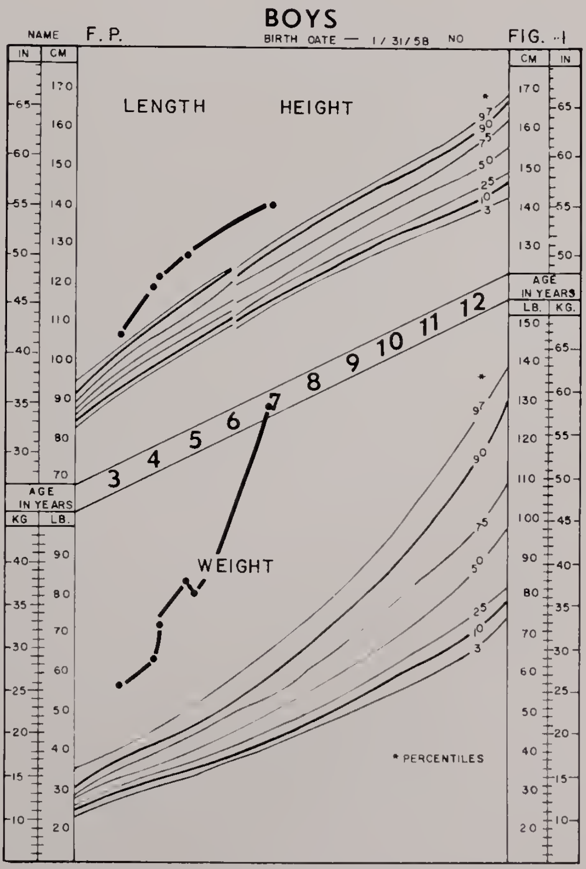

Fig. 4 — Maximum linear growth spurt is seen between ages 3½ and 4½ years.

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*See Test Your Word Score Page 1639.

Summary

A case of excessive growth in childhood has been presented. This patient demonstrates anatomic and developmental features which appear identical with a previously described group. The present case differs from the earlier ones in that there are quantitative abnormalities of adrenal hormone production, which are considered secondary to the manifest central nervous system disorder. Anatomical considerations support the citation of this case as a variant of the disease previously reported as cerebral gigantism.

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IT'S THE LAW

Deductibility of Travel Expenses as Educational Expenses

Travel expenses necessarily incurred are deductible as educational expenses if the taxpayer can show that his itinerary was chosen and the major portion of his activities during the trip was undertaken for the primary purpose of maintaining or improving skills required in his business or profession. However, problems arise when, in the course of vacation travel, side-trips are taken to places where the taxpayer may receive knowledge which may be of educational value to him in his business or profession. For example, an American surgeon might be benefited in his profession by observing the performance of a delicate operation by a renowned European surgeon, or an American lawyer might profit by watching English barristers conducting a trial. These isolated deviations from their vacation travels would not entitle them to deduct all of their travel expenses. The extent to which travel expenses would be deductible, as educational expenses, would depend on the facts of the particular case.

Cross v. U. S., 336 F. 2d 431 (C.A. 2. Aug. 7, 1964) — Citation Jan. 29, '65.

Astrology and Medicine

The sun is a fiery and cardinal astrological sign. Disturbances in its vital, expansive force result in corresponding disturbances in those physiological functions that are solar-controlled, principally those involving the heart, the spine, and the spleen. The moon is a watery, mutable sign. When afflicted it disposes to complaints resulting from disorders of the body fluids and mucous membranes, and also to female disorders and pathologies of periodic manifestation.

The sun's energy is electric, the moon's magnetic.

Drawing on my fine command of language, I said nothing. — Robert Benchley

Dialysis Therapy on a Medical Service*

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In 1877 Wegner demonstrated that irrigation of the peritoneum of rabbits with concentrated sugar solution would permit the collection of a larger volume of fluid than had been initially instilled.[1] During the next 40 years several investigators showed that the intraperitoneal injection of hypotonic solutions in rabbits and dogs was followed by a rapid depletion of the volume of instilled fluid. It was also shown that solute could pass across the peritoneal membrane, the direction of net flux being determined by the concentration gradient. Numerous attempts to substitute for failing renal function by employing the semipermeable membranes of the body to effect transfer of accumulated body urea into rinsing fluids were reported from 1920 through 1940. The stomach, small intestine, pleural cavity, lung, bladder, and vagina were tested for their suitability as dialyzing surfaces, but the most promising body cavity appeared to be the abdomen because of the large surface area, approximately two square meters in man, of the serosal peritoneum.

Grollman, Turner and McLean in 1951 reported that bilaterally nephrectomized dogs which usually live a maximum of three to five days could be kept alive up to 70 days by repeated peritoneal dialysis.[2] This experimental observation found clinical application in the 1953 study of LeGrain and Merrill which noted that short-term continuous peritoneal irrigation was an effective method of removing solute and water from the oliguric patient with concomitant prolongation of life.[3] The development of disposable plastic cannulas and the commercial availability of

TABLE I

	Predialysis 144	Postdialysis 138
Blood Pressure, mm. Hg.	90	80
Weight-pounds	119	116
BUN, mg/100 ml.	88	30
Creatinine, mg/100 ml.	11.1	5.2
Arterial CO_2 content, mEq/L	18.5	32
Na^+, mEq/L	136	140
K^+, mEq/L	6.2	4.2
Cl^-, mEq/L	105	99
Ca^{++}, mg/100 ml.	7.4	10.2
$PO_4^{\equiv}$, mg/100 ml.	6.4	4.7
Hematocrit, per cent	25	28

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peritoneal dialysis solutions in 1958 stimulated further interest in the possible applications of this method of dialysis. Peritoneal dialysis is now accepted as both an important addition to the therapy of renal failure and a useful technique for clinical investigations of solute transfer across a semipermeable membrane.

Simultaneous with the clinical demonstration of the practicability of peritoneal dialysis in cases of impaired renal function were the continued attempts to develop a technique for the extracorporeal dialysis of blood. It was not until 1944 that Kolff (while working under the handicap of the German occupation of his native Holland) devised the first workable artificial kidney[4] by utilizing cellophane sausage casing as a semipermeable membrane through which the patient's arterial blood, with heparin added to retard clotting, was circulated. The blood-filled cellophane tubing was wrapped around a rotating drum which dipped into a 100-liter dialysis bath. Exchange of solute and water was effected prior to the return of the blood to a convenient vein. Shortly after World War II, rotating-drum artificial kidneys (with minor modifications of the prototype) were evaluated at several centers in the United States. Merrill[5] and Schreiner[6] at midcentury collected series of cases demonstrating the effective and often lifesaving use of hemodialysis in the treatment of acute renal failure and certain drug overdosage.

Later modifications of the instrument of hemodialysis were aimed at lessening the burden of preparation of the unit and reducing the size of the blood compartment with the purpose of reducing the cost and hazards of priming with blood. The size of the apparatus necessary to effect hemodialysis was considerably diminished by winding two lengths of cellophane tubing supported by plastic window screening around a beer can to produce the now well known twin-coil artificial kidney. A disposable coil unit for this type of dialyzer has been commercially available for a decade. The need for blood priming in and pumping through the large-volume high-resistance twin-coil unit led to the search for lower-volume, low-resistance dialyzers, the most efficient of which is the Kiil parallel-flow artificial kidney. Among the 300 artificial kidneys estimated to be currently in use in the United States can be found rotating drums, twin coils, and parallel-flow Kiil dialyzers. In this report, examples of several of the many applications of dialysis therapy on a medical service will be illustrated.

Peritoneal Dialysis

Peritoneal dialysis can be performed by a specially instructed nurse after the abdominal puncture wound is made and the apparatus is properly set in operation. Improved abdominal access trocars and inexpensive, disposable, small-diameter nylon catheters permit the insertion of the dialysis cannula under local anesthesia, in the patient's room. After the abdominal wall is shaved and disinfected, a one-centimeter circular area approximately one third of the distance between the umbilicus and pubis is infiltrated with one-per-cent procaine. A number 11 knife blade is used to make a three to five-millimeter skin incision in the anesthetized area through which a 14F trocar is inserted into the abdominal cavity. A nylon catheter is introduced through the trocar, the trocar is removed, and the catheter taped to the abdominal wall. Two liters of dialysate, warmed to body temperature, are allowed to run into the abdominal cavity by gravity flow during a ten to twenty-minute period. After an equilibration time of approximately twenty minutes the fluid is drained into a collection bottle by gravity flow. When indicated, removal of excess fluid from the patient can be accomplished by increasing the osmolality* of the dialysate. An increase in the glucose concentration of the dialysate from 1.5% to either 4.25% or 7% will cause an increase in the return volume of as much as three liters for each two liters instilled. The entire cycle of inflow, equilibration and drainage can be completed in one hour, at which time two liters of fresh dialysate are introduced into the peritoneal cavity and the cycle is repeated. At a flow rate of two liters per hour peritoneal urea clearances of 15 to 25 milliliters per minute are obtained. A

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*See Test Your Word Score Page 1639.

24-hour dialysis at a flow rate of two liters per hour will usually result in a blood urea nitrogen of half the predialysis level.

Acute Tubular Necrosis

Case 1 illustrates the use of peritoneal dialysis in renal failure of undetermined etiology.

Case 1

A twenty-four-year-old negro male heroin addict was hospitalized because of fever and hemoptysis. The patient had allegedly lain unattended in a street for two days after being assaulted. At the time of admission he was poorly responsive and somnolent. Significant findings on physical examination included two + pitting edema of the legs, flatness to percussion of the right posterior chest and tubular breathing and moist rales throughout the posterior right lower lung field. Radiographic examination of the chest disclosed infiltration and cavitation of the right upper lobe and a right pleural effusion.

The white blood count was 22,800 per cu. mm., the hemoglobin 12 gm. per 100 ml.; the urine gave a 1+ test for protein; the sediment contained three red cells and a rare white cell per high power field. The blood urea nitrogen was 200 mg. per 100 ml. and the serum creatinine 9.5 mg. per 100 ml.

During the first hospital day the patient's urinary output was 275 ml. Sequential electrocardiograms showed peaking of the T waves and spreading of the QRS complex indicative of the development of progressive potassium intoxication. Intravenous penicillin therapy, 1.2 million units every four hours, was administered for the pneumonia, and intermittent peritoneal dialysis at a flow rate of two liters per hour was performed during the next two hospital days with a total exchange of 80 liters in 40 hours. By the use of hypertonic dialysis solution with a glucose concentration of 4.25% an excess of 15 liters was removed from the patient with consequent clearing of his edema and a resultant weight loss of 20 pounds. At the end of the dialysis the blood urea nitrogen was reduced to 109 mg. per 100 ml. and the electrocardiogram reverted to normal.

A percutaneous right renal biopsy was obtained on the third hospital day and was consistent with extensive acute tubular necrosis (Figure 1).

Following the peritoneal dialysis the patient developed a sustained diuresis associated with continuing improvement in his renal function. Clinically and radiologically the lung disease resolved during the next three weeks. At the time of discharge on the 43rd day the patient's blood urea nitrogen was 14 ml. per 100 ml. and his endogenous creatinine clearance was 114 ml./minute.

Until the interpretation of the renal biopsy in Case 1 it was not clear whether the patient's diagnosis was acute renal failure due to tubular necrosis, acute glomerulonephritis, or oliguria as a consequence of chronic renal disease.

The over-all mortality from acute tubular necrosis varies from 20 per cent to 80 per cent, depending on the cause. Deaths due to potassium intoxication, intravascular congestion and uremic pericardial tamponade can be prevented by the incorporation of properly timed peritoneal dialysis into the regimen of care for the patient with acute reversible renal failure.

Prolonged Anuria

Peritoneal dialysis can be performed repeatedly in cases of prolonged anuria due to potentially reversible renal failure (Case 2).

Case 2

A 37-year-old Puerto Rican mother of five was hospitalized for the first time because of convulsions, hypertension and pulmonary edema. Ten days previously she had suffered a two-day "bad cold" associated with fever and pharyngitis. Because of confusion, intravascular congestion, and hyperkalemia,

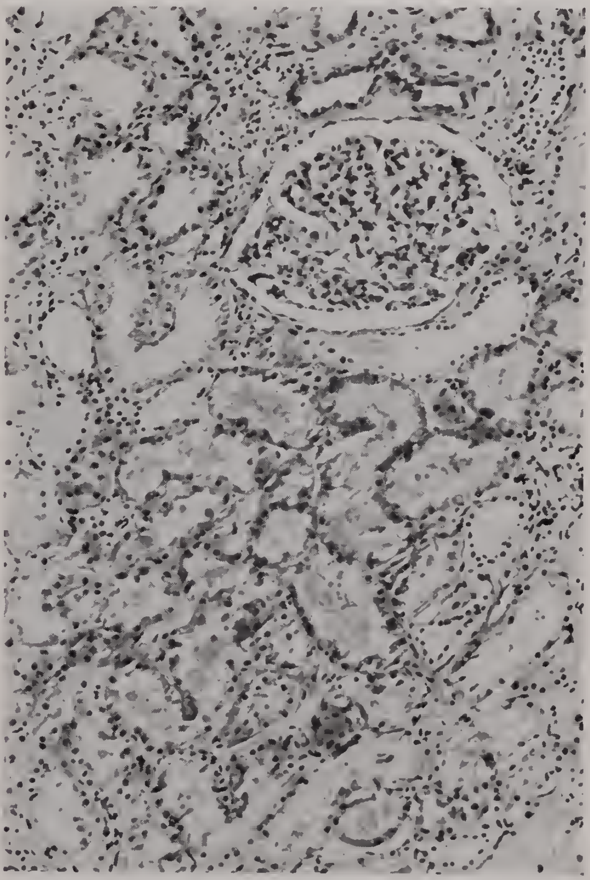

Fig. 1. Case 1 — Acute tubular necrosis. Cortical area of kidney showing tubular epithelium in varying stages of degeneration. Some tubules have an incomplete epithelial covering. Hematoxylin and eosin. X 200.

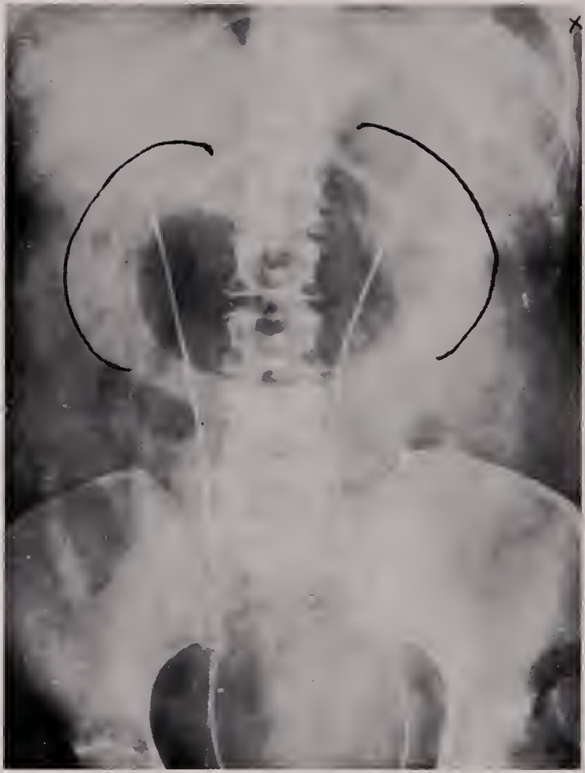

Fig. 2. Case 2 — Both kidneys are swollen and measure 15 cm. in length. The ureters are patent.

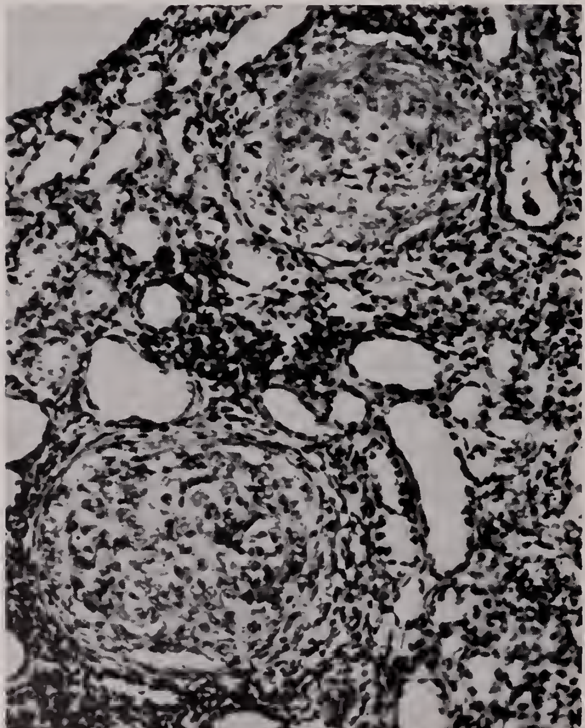

Fig. 3. Case 2 — Acute glomerulonephritis. Two glomeruli showing marked hypercellularity of the tufts with almost complete obliteration of Bowman's space. Hematoxylin and eosin. X 200.

intermittent peritoneal dialysis with hypertonic dialysate was begun shortly after admission. The initial dialysis resulted in a reduction of the blood urea nitrogen from 140 to 75 mg. per 100 ml. and a fall in the serum potassium from 6.6 to 4.2 milliequiv. per liter. On the third hospital day, because the patient was anuric, bilateral ureteral catheterization was performed and patency of both ureters was demonstrated. The tentative diagnosis of post-streptococcal glomerulonephritis was substantiated by the finding of enlarged kidneys, measuring 15 cm. each (Figure 2), an elevated antistreptolysin 0 titer of 833, and a percutaneous biopsy of the right kidney (Figure 3).

Although ambulatory, afebrile and comfortable, the patient remained totally anuric. Three peritoneal dialyses were required to control her uremic symptoms during the first fifteen days of her hospitalization. It was then decided to place the patient on a regimen of weekly peritoneal dialysis in hospital while she remained at home with her family for six days of each week. A 14F nylon catheter was left in the peritoneum and the patient was discharged with instructions to follow a 40-gram protein, 400 mg. sodium, 2,500 calory diet. To increase bowel excretion of dietary potassium 50 grams of a potassium exchange resin and 40 ml. of sorbital were prescribed daily.

For the ensuing five months, though totally anuric and mildly hypertensive, the patient remained at home with her family preparing meals and caring for her children. Active destruction of renal mass continued throughout this period as evidenced by the marked reduction in renal size seen in nephrotomograms taken three months after the onset of illness (Figure 4).

The patient's blood urea nitrogen (Figure 5) and serum potassium (Figure 6) were effectively controlled for five months by weekly peritoneal dialysis, but relentless weight loss (Figure 7) continued until the patient's sudden death at home three days after her last peritoneal dialysis, during the 24th week of her illness. An autopsy was not performed.

Reports of recovery of renal function after as long as 28 days of anuria due to post-streptococcal glomerulonephritis have been confirmed.[7] At what point in the proper management of acute glomerulonephritis is dialysis to be discontinued? Should dialysis be stopped even though the anuric patient is in satisfactory medical condition? How long can peritoneal dialysis be continued without technical failure? These questions are the subject of active investigation and are only partially answerable at this time.

Complications of Dialysis

Protein Loss

Complications have limited the survival of most functionally anuric patients to about six months. Josephson and Friedman detected as much as 1½ grams of plasma protein, principally albumin, per liter of peritoneal dialysate, a quantity difficult to replenish by increased dietary intake of proteins. Boen has infused intravenously the ascitic fluid found at the start of each dialysis and thus limited the protein-wasting. We have infused 25 grams of salt-poor human albumin twice monthly with satisfactory preservation of plasma albumin concentration at 3.5 grams per 100 ml. into a patient now in his sixteenth month of intermittent peritoneal dialysis performed at seven-day intervals.

Peritonitis

The incidence of bacterial peritonitis can be markedly reduced by strict attention to aseptic technique and the use of a fresh puncture for each dialysis. Antibiotics are added to the dialysate only when the signs of peritonitis are present and are changed to suit the sensitivity of any cultured organism.

It is obvious that the regular cycling of two liters of dialysis fluid per hour over any several days can prove a burdensome chore. In order to lessen the labor of peritoneal dialysis and increase its efficiency, automatic machines have been devised by Boen[8] and McDonald.[9] The McDonald peritoneal dialysis apparatus supplants gravity flow by pumped inflow and outflow, achieving exchanges as high as eight liters per hour with urea clearances of 35 to 50 milliliters per minute.

Improved techniques for performing peritoneal dialysis and conserving plasma proteins will result in a decreased morbidity and mortality due to this procedure.

Hemodialysis

Hemodialysis is a more complex procedure than peritoneal dialysis. Connections must be established between the dialysis apparatus and the patient's blood vessels. Because of the necessary vascular surgery, and because rapid changes in the patient's clinical state are effected by this more efficient procedure, a team of physicians and nurses is required to care for the acutely-ill patient subjected to hemodialysis.

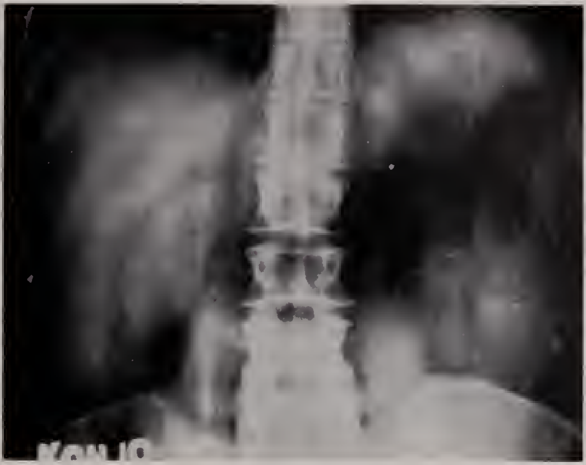

Fig. 4. Case 2 — Three months after the onset of acute glomerulonephritis the kidneys are reduced in size to 7 and 8 cm. in length.

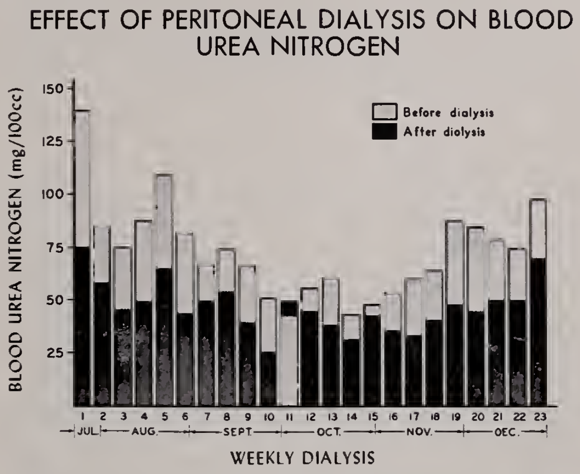

Fig. 5. Case 2 — The patient's blood urea nitrogen was generally maintained between 50 and 100 mg. per 100 ml. throughout the five months of dialysis.

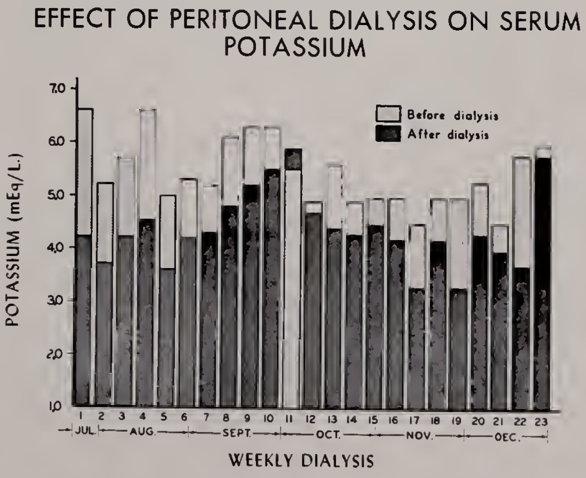

Fig. 6. Case 2 — Prior to each weekly dialysis hyperkalemia was present.

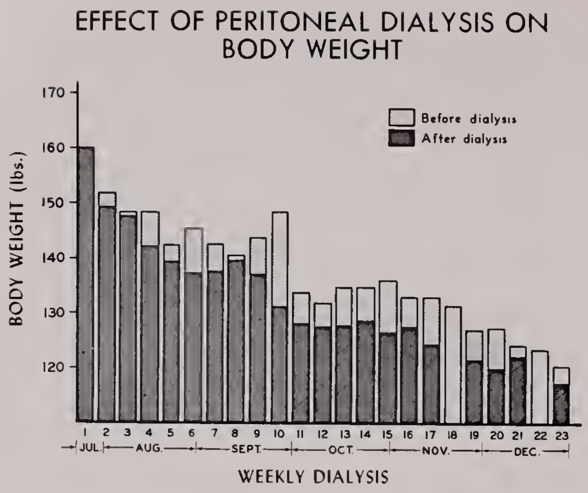

Fig. 7. Case 2 — Progressive weight loss of 40 pounds in five months of peritoneal dialysis was related to restricted protein ingestion and protein wastage in the dialysate.

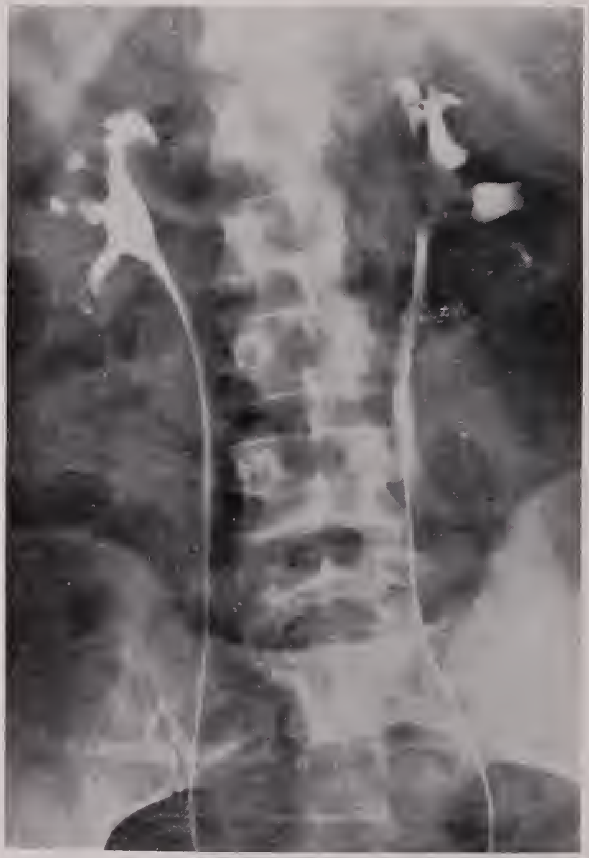

Fig. 8. Case 4 — Both kidneys are reduced in size. They have distorted collecting systems and thin parenchyma consistent with chronic pyelonephritis.

Drug Intoxication

One of the most successful applications of hemodialysis has been in the treatment of drug intoxications. The list of dialyzable poisons is constantly growing and has been most recently revised by Maher in 1964.[10] Case 3 is an example of the effective use of hemodialysis to treat a patient who ingested an overdose of a dialyzable sedative.

Case 3

A twenty-two-year-old unemployed white male stock clerk was transferred from another hospital approximately six hours following the ingestion of twenty-seven 0.5 gm. tablets of glutethimide (Doriden). The patient was comatose and had neither the corneal nor gag reflex. During the initial two-hour period of observation his coma deepened and he became hypotensive with a blood pressure of 80 systolic and 20 diastolic. A double-lumened nylon catheter was passed through the right long saphenous vein into the inferior vena cava yielding a blood flow of 300 ml./minute. Hemodialysis was performed through a Kolff twincoil artificial kidney primed with two units of bank blood.

The patient's response to hemodialysis was rapid. By the third hour his corneal and gag reflexes had returned and by the fifth hour flailing movements of his extremities were present. At the conclusion of six hours of hemodialysis the patient was sufficiently alert to give his own medical history. Thereafter his recovery was uneventful, and in collaboration with a consulting psychiatrist the patient was discharged on the fourth hospital day to the outpatient clinic.

Uremia

Hemodialysis will produce improvement in the signs and symptoms of uremia, whether due to either acute or chronic renal failure. Until the development by Scribner of a method for indwelling long-term arterial and venous cannulation, however, the number of hemodialyses which could be performed on patients was limited by the availability of peripheral blood vessels. Scribner devised indwelling silicon-elastic and teflon cannulas which allowed for repeated use of the same artery and vein over months or years.[11] Arterial blood is externally shunted to a vein in the arm or leg without the necessity for the use of anticoagulants except during periods of hemodialysis. Case 4 is a patient who has had such a shunt in place for thirteen months.

Case 4

A 32-year-old white housewife was hospitalized at the Kings County Medical Center for the first time in October 1964 because of azotemia and hypertension. Her only pregnancy eight years earlier, although complicated by hypertension and edema, produced a full-term healthy son. Episodic back pain, fever and dysuria interrupted her work as a bookkeeper with increasing frequency during the next few years and culminated in sustained nausea, vomiting, somnolence and oliguria, which necessitated her admission to another hospital in June of 1964. A 48-hour peritoneal dialysis performed at that time induced a partial remission and the patient was discharged. She remained at home, however, suffering from nausea and lethargy until a convulsion caused a second hospitalization in August 1964. Therapy consisted of short-term peritoneal dialysis with hypertonic dialysate which resulted in considerable diminution in the patient's nausea and an improved sensorium. She then remained home for seven weeks until the onset of convulsive seizures and pulmonary edema required a third hospitilization. Following an uncomplicated peritoneal dialysis with remission of her uremic symptoms the patient was transferred for further therapy.

Physical examination at the time of admission disclosed a drowsy, cooperative woman appearing acutely and chronically ill. She was deeply pigmented and had 3+ pitting edema of the legs and sacrum. The blood pressure was 180 systolic, 108 diastolic. Her hemoglobin was 6.8 gm. per 100 ml.; the white blood count was 10,800 cu. mm. with a normal differential count. A urinalysis revealed 2+ protein, 0 to 1 red blood cells, and 12 to 15 white blood cells per high power field. Two urine cultures grew enterococcus organisms. Both kidneys were contracted with marked loss of cortical tissue consistent with chronic pyelonephritis (Figure 8); a percutaneous biopsy of the right kidney confirmed this diagnosis (Figures 9, 10). It was apparent from the endogenous creatinine clearance of 1.6 ml./ minute that the patient's residual renal function was insufficient to sustain life.

Accordingly, a silastic-teflon arterial venous shunt was inserted into the left radial artery and vein to allow for repeated hemodialysis (Figures 11, 12). The patient has been maintained for thirteen months by a program of twice weekly night-time hemodialysis utilizing a low pressure, nonpriming Kiil parallel-flow artificial kidney. Since her discharge in December 1964 she has resumed her household responsibilities and has been clinically well, with a gradual weight gain of 17 pounds. Her therapeutic regimen consists of a 40-gram protein 400 mg. sodium 2,500 calorie diet with no other medications. Her urine output varies from 50 to 100 ml. daily.

Table 1 lists this patient's pre- and postdialysis blood chemical values for a typical eleven-hour hemodialysis.

Complications

Intermittent hemodialysis substitutes for only a few of the complex functions performed by the healthy kidney. The rehabilitated patient remains anemic and colored by urochrome pigment in his skin. He may develop arthritis, peptic ulceration, peripheral neuropathy or secondary hyperpara-

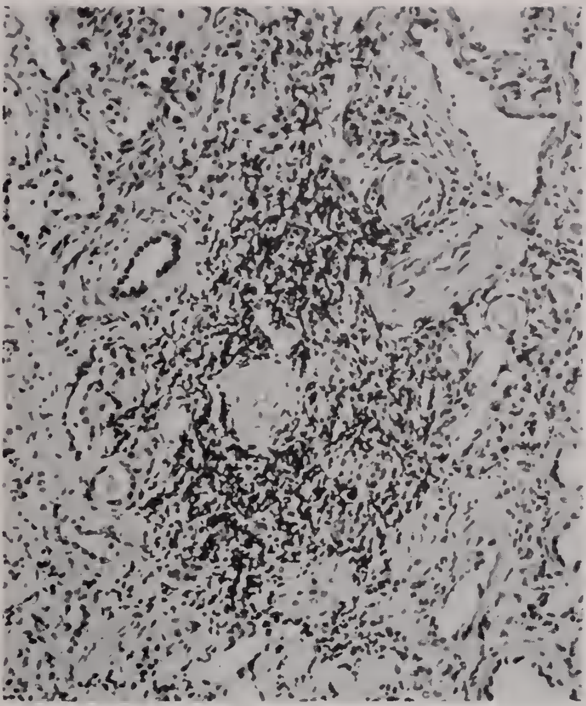

Fig. 9. Case 4 — Medulla of kidney showing interstitial fibrosis, round cell infiltration, vessels with arteriosclerosis and tubules, changes consistent with chronic pyelonephritis. Hematoxylin and eosin. X 400.

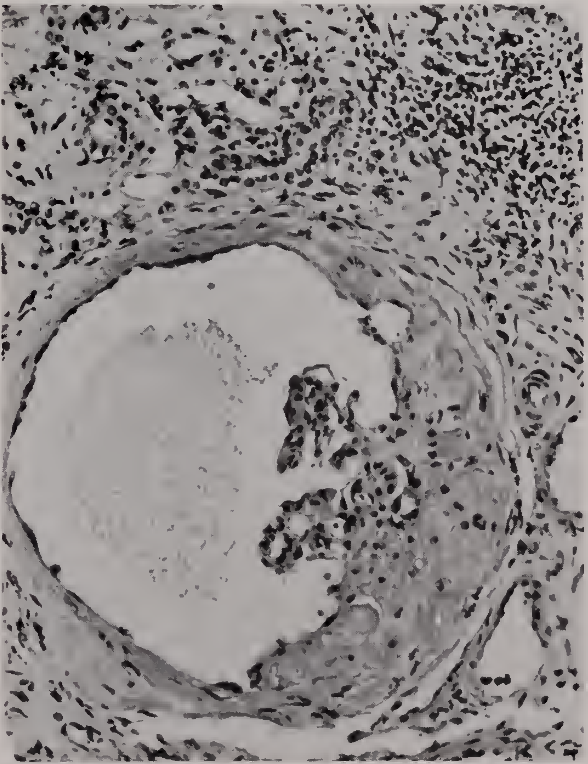

Fig. 10. Case 4 — Glomerulus from the same biopsy as Figure 9, with pericapsular thickening and round cell infiltration in the interstitium. Hematoxylin and eosin. X 400.

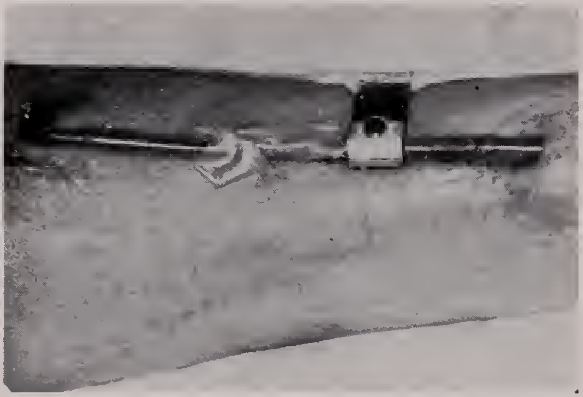

Fig. 11. Case 4 — The cannulated forearm vein (left) and radial artery (right) have shunted blood flow through the silastic-teflon connectors.

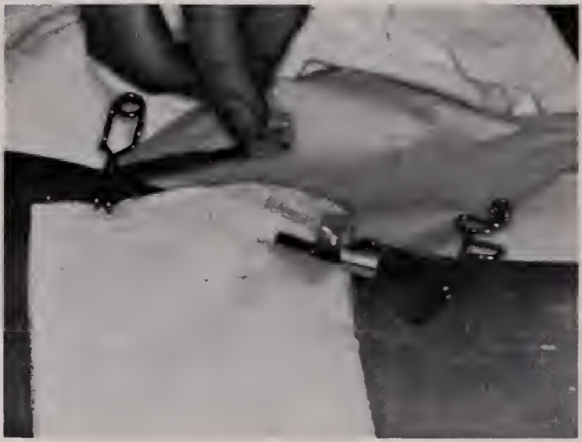

Fig. 12. Case 4 — In preparation for hemodialysis the shunt is opened. The compressible silastic portion of each cannula is clamped and the teflon connectors are fitted into the dialyzer tubing. The arterial cannula is on the right of the photograph.

thyroidism. His requirement for blood transfusions exposes him to inoculation with the virus of hepatitis.

Case 5

A 43-year-old white married businessman developed end-stage renal failure and anuria due to chronic glomerulonephritis. For five months, while receiving twice weekly hemodialysis with a Kolff twin-coil artificial kidney primed with bank blood, he remained out of hospital and able to run his dress factory. He was normotensive and had regained eight pounds when, during the sixth month of dialysis, he contracted fulminant hepatitis which necessitated hospital readmission. Progressive jaundice and a clouded sensorium were not altered by either corticosteroid therapy or an eight-hour hemodialysis. The patient died two days later while in liver coma. Autopsy examination showed extensive necrosis of the liver consistent with the diagnosis of viral hepatitis.

Comments and Conclusions

Despite the medical and psychological limitations of a life dependent on a machine, the patient subjected to chronic intermittent hemodialysis has much more than just a gloomy alternative to death. The majority of patients return to their jobs, schools or homes on a near full-time basis.

Approximately 200 patients with "end stage" uremia are receiving this form of therapy today.

Whether the treatment of choice for chronic renal failure a generation from now will involve the transplantation of a cadaver or animal kidney, or the insertion into the abdomen of a small artificial kidney made of a plastic yet to be devised, is highly speculative. What is clear is that the physician with an interest in uremia can more hopefully expect an increasingly brighter prognosis for his patients.

Acknowledgments

The dialysis unit at the Kings County Medical Center is a combined venture of the medical and urology services. Dr. R. Keith Waterhouse and Dr. Harold McDonald, Jr., collaborated in the care of the patients reported, Dr. Gerald E. Thomson in the studies of the patients subjected to hemodialysis, and Dr. Stanley Minkowitz with the pathology of the renal biopsies.

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Education: that which discloses to the wise and disguises from the foolish their lack of understanding. — Bierce

Megaloblastic Anemia of Infancy

- Response to a
- Minimal Dose
- of
- Pteroylglutamic Acid

MARGARET G. ROBINSON, M.D.*
Brooklyn, New York

THE DAILY minimal requirement and the minimal therapeutic dose of folic acid are unknown. The usual therapeutic dosage ranges from 0.4 to 10 mg. per day. A few workers have used minute doses of the order of 25 to 50 ug. of folic acid daily to determine the minimal therapeutic dose for adults.[1-4] Although the response to therapy was delayed, these minute doses have cured folic-acid deficiency. Since the minimal therapeutic dose is close to the minimal daily requirement, Zalusky and Herbert,[1] on the basis of one case report, have suggested that the minimal daily requirement of adults for the free form of folic acid is probably of the order of 50 to 100 ug. per day.

No similar work has been performed on infants. We have attempted to determine the probable range of the minimal therapeutic dose and, indirectly, the minimal daily requirement of folic acid in a five-month-old infant. The therapeutic response obtained with the daily administration of 50 ug. of pteroylglutamic acid while the child was maintained on a folic-acid-free diet would indicate that the minimal therapeutic dose and minimal daily requirement of the free form of folic acid for infants are equal to or less than 50 ug. per day.

Methods

Standard methods were used for the determination of complete blood counts every three to four days.[5] Reticulocyte counts were made daily, using brilliant cresyl blue. Bone-marrow aspirates were obtained from the tibia or the anterior iliac crest. Folic-acid plasma clearance tests were performed by the method of Herbert and Zalusky[6] by giving 15 ug. per kg. body weight of folic acid

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Editor's Note: Dr. Robinson received her B.A., Magna cum Laude from the University of Minnesota in 1950, taught bacteriology and chemistry at the Kohler School of Nursing two years, and received her M.D. in 1956 from the University of Minnesota.

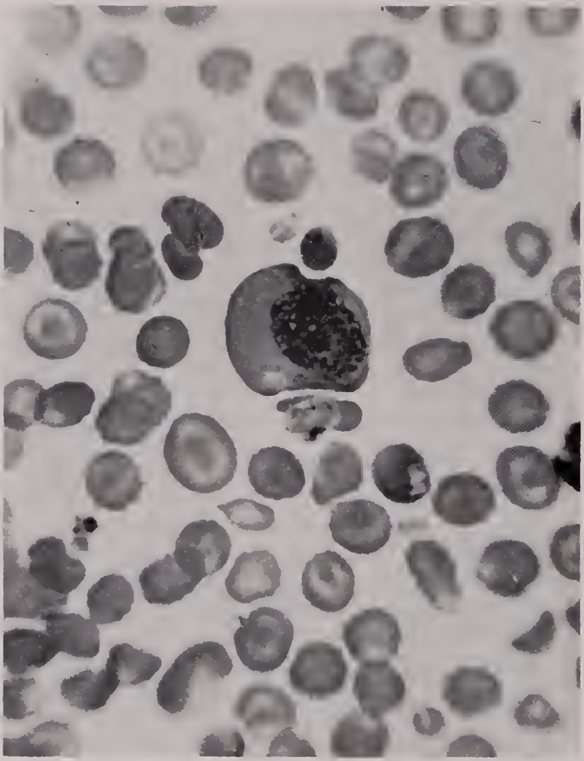

Fig. 1 — Peripheral blood smear demonstrating megaloblastic changes in nucleated erythrocyte and rare macrocytes (x 1000).

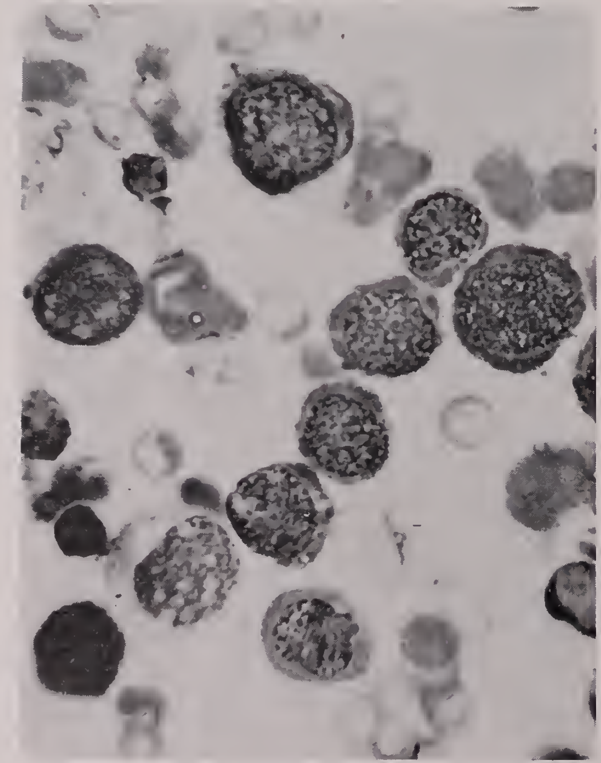

Fig. 2 — Bone marrow prior to therapy illustrating the promegaloblasts and basophilic megaloblasts (x 1000).

intravenously. Serum was obtained at 15 and 30 minutes after the intravenous injection and assayed microbiologically using Lactobacillus casei by the aseptic method of Herbert et al.[7]

Case Report

An 11-week-old premature, negro female infant was admitted to Kings County Hospital for diarrhea of five days' duration. Nonprojectile vomiting and fever (39.4°C.) had begun two days prior to admission. Her birth weight was 2.5 kg. During the first month of life she was treated for an omphalitis and an acyanotic heart disease. At eight weeks of age she received two weeks of penicillin therapy for a right middle lobe pneumonia. Her diet consisted of 15 oz/day of Similac® formula and Tri-vi-Sol® 0.6 cc. daily (containing 60 mg. ascorbic acid). The family history was noncontributory.

Physical Findings

The physical examination showed a moderately dehydrated infant weighing 3 kg. Her temperature was 37°C; respiratory rate, 44/min.; pulse, 160/min. There was a grade 3 systolic murmur at the left of the sternum, maximal in the third intercostal space and radiating into the axilla. The patient was lethargic. The remainder of the physical examination was within normal limits.

The hemogram showed a hemoglobin of 8.5 gm% with a leukocytosis (Table 1). Stool cultures were positive for enteropathogenic E. coli, type 0111 B4. The admission chest roentgenogram showed only increased pulmonary markings.

During the next 12 weeks she had six bouts of diarrhea treated with neomycin and colymycin, a purulent conjunctivitis treated with neosporin ophthalmic ointment, and a diffuse pneumonia involving the entire right lung and left upper lobe, which was treated with penicillin. Intravenous fluid therapy was used to correct hydration and acidosis. Between each episode of diarrhea her diet consisted of Similac® formula and Tri-vi-sol® 0.6 cc. daily.

Diagnostic Studies

At 23 weeks of age during her sixth episode of diarrhea she developed increasing pallor and unresponsiveness to therapy. Examination of her blood showed a hemoglobin of 5.8 gm% (Table 1). Some macrocytes, a rare hypersegmented neutrophil and a few nucleated erythrocytes with minimal megaloblastic changes were seen on the peripheral blood smear (Figure 1). Following a transfusion of 40 cc. of whole blood her hemoglobin was 7.2 gm% and her reticulocyte count, 0.4%. The pretherapy bone marrow was megaloblastic (Table 2 and Figure 2). A folic-acid plasma clearance study performed on the first day of therapy using a total dose of 54 ug. of pteroylglutamic acid was abnormally rapid (Table 3). A diagnosis of folic-acid deficient megaloblastic anemia was made.

Therapy

She was given 50 ug. of folic acid intramuscularly every day. During the first 10 days of folic-acid therapy the child was being hydrated with intra-

TABLE 1
Hemograms During the 2 Hospitalizations of the Patient*

	1st Admission	Pre-folic Acid Therapy	2nd Admission
Hemoglobin (mg%)	8.5	5.8	7.2
RBC (x 10^6/cu. mm.)		1.84	4.47
Hematocrit (%)		19.0	27.0
MCV (cu.u)		100.3	61.0
MCHC (%)		30.4	26.5
MCH (u.u)		31.5	16.0
Reticulocytes (%)		0.2	1.4
Platelets	Adequate	Adequate	Adequate
WBC (per cu. mm.)	22,950	14,300	
Neutrophils	5	35	
Stabs	14	2	
Lymphocytes	78	54	
Monocytes	2	7	
Eosinophils	1	1	
Basophils		1	
Nuc. RBC/100 WBC		3	
Sickle cell preparation		Negative	

*See Fig. 3 for other hematological data while on folic-acid therapy.

TABLE 2
Bone-Marrow Differentials

	Pretherapy	7th Day of Therapy	22nd Day of Therapy
Myeloblasts	2.0	2.0	2.0
Promyelocytes	2.5	1.3	1.5
Myelocytes	6.5	8.0	6.0
Metamyelocytes	19.0	14.7	33.0
Mature neutrophils	3.0	2.0	18.0
Eosinophils	1.0	1.3	2.0
Lymphocytes	15.0	13.3	4.5
Pronormoblasts	1.0		1.0
Basophilic normoblasts	3.5	1.3	2.0
Polychromatic normoblasts	5.0	8.0	5.0
Orthochromic normoblasts	4.0	41.0	24.0
Promegaloblasts	9.0	0.7	0.0
Basophilic megaloblasts	13.5	0.0	0.0
Polychromatic megaloblasts	11.5	0.7	0.0
Orthochromatic megaloblasts	4.0	5.7	0.0
Mitotic figures	1	3	2
Myeloid: erythroid ratio	1:1.5	1:1.9	2:1

Comments: The majority of the neutrophilic metamyelocytes in the first bone marrow and approximately 1/3 of the metamyelocytes in the second bone marrow were giant metamyelocytes. Normal, functioning megakaryocytes were present in all bone-marrow specimens. Plasma cells were found on all bone-marrow specimens.

TABLE 3
Folic-acid Plasma Clearance Studies

	15 minutes	30 minutes
Normals	80 — > 300 mug/cc.	50 — 200 mug/cc.
1st day of therapy	13 mug/cc.	11 mug/cc.
10th day of therapy	80 mug/cc.	75 mug/cc.

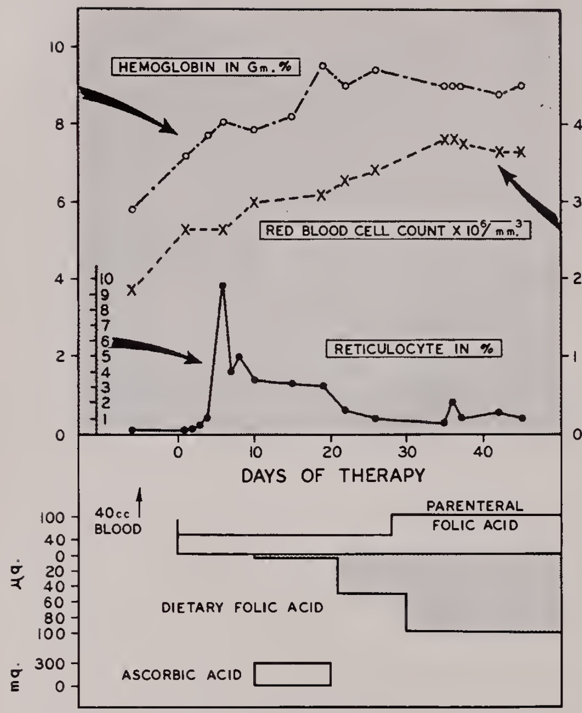

Fig. 3 — Hematological response to folic acid of a five-month-old premature infant with megaloblastic anemia.

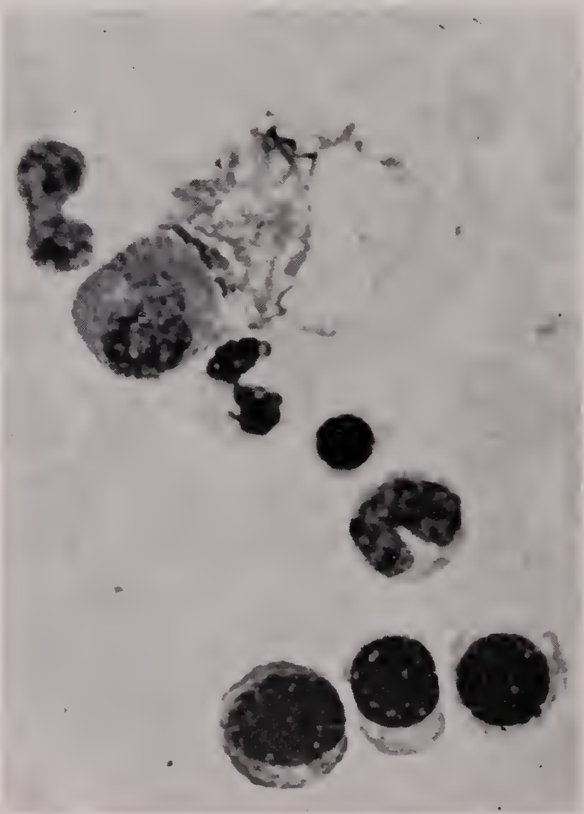

Fig. 4 — Bone marrow on 22nd day of therapy showing the typical polychromatic normoblasts (x 1000).

venous fluids and oral electrolyte solution. No formula, solid foods or supplementary vitamins were given. A peak reticulocyte response of 9.6% was reached on the sixth day of therapy (Figure 3). On the seventh day the bone marrow still showed minimal megaloblastic changes in the erythroid series and giant metamyelocytes (Table 2). A folic-acid plasma clearance test on the 10th day of therapy showed borderline normal values (Table 3).

Between the 10th and 20th days of folic acid therapy her diet consisted of 300 mg. ascorbic acid and 500 cc. of Similac® daily, with no evidence that the vitamin C influenced the reticulocyte count (Figure 3). Her hemoglobin rose to 9.5 gm% by the 20th day. A bone marrow performed on the 22nd day of folic-acid therapy demonstrated a normoblastic marrow (Table 2 and Figure 4). Her red cell count rose from 2,630,000/cu. mm. on the first day of therapy to 3,800,000/cu.mm. on the 38th day. The dietary and parenteral folic acid were increased to 100 and 200 mg./day on the 20th and 28th days of therapy respectively without any further rise in reticulocytes or hemoglobin (Figure 3).

Because her peripheral blood smear showed mild hypochromia, oral iron supplements to the diet were recommended. She failed to return to clinic following her discharge. At 13 months of age when she was readmitted for pneumonia and congestive heart failure she had an iron deficiency anemia (Table 1). Following a total dose of 300 mg. of elemental iron given intramuscularly, her hemoglobin at 14 months of age was 12.0 gm% and her peripheral blood smear was normocytic and normochromic.

Discussion

In the past, *differentiation of folic-acid deficiency from vitamin B_{12} deficiency* has been made by therapeutic trial, using 0.4 to 10 mg. of folic acid. The use of a therapeutic trial for differentiating these two forms of megaloblastic anemia has a serious disadvantage. By mass action, folic acid given in daily doses of 1 to 10 mg. will convert to normal a megaloblastic marrow due to vitamin B_{12} deficiency. Only vitamin B_{12} will prevent or arrest the development of the neurologic changes associated with pernicious anemia. The daily administration of even as small a daily dose as 0.4 mg. of folic acid can revert the megaloblastic marrow of vitamin B_{12} deficiency to normal without preventing the central nervous system complications of pernicious anemia.[8]

One method of preventing the masking of a pernicious anemia by the use of folic acid would be to treat all patients who have megaloblastic anemia with both folic acid and vitamin B_{12}. Since pernicious anemia is a life-long condition this would necessitate continuous therapy with vitamin B_{12} in all cases of megaloblastic anemias. A second and more practical method to solve this problem would be to find a small enough dose of folic acid that would be just sufficient to cure folic-acid deficiency without altering the hematological picture in vitamin B_{12} deficiency.

Because of this danger of *masking a vitamin B_{12} deficiency with the usual therapeutic dosages of folic acid,* a few workers have attempted to find the minimal therapeutic dose of folic acid. Using 25 to 50 ug./day, these workers have successfully treated folic-acid-deficient megaloblastic anemia associated with anticonvulsants, scurvy, sprue and pregnancy in adults.[1-4] All the patients except one received additional folic acid in their diet. The patient reported by Zalusky and Herbert[1] responded to the daily administration of 50 ug. of pteroylglutamic acid while being maintained on a folic-acid-free diet. The delayed but complete responses to these minute dosages of folic acid would indicate that the minimal therapeutic dosage was in the range of 50 to 100 ug. per day and that the minimal daily requirement was equal to or less than this for adults. No similar work has been done on infants.

To determine the range of the minimal therapeutic dose and the range of the daily minimal requirement of this vitamin for infants, we administered 50 ug./day of pteroylglutamic acid parenterally while maintaining our five-month-old patient on a folic-acid-free diet. The diagnosis of folic-acid-deficient megaloblastic anemia was made in this patient by the finding of a megaloblastic marrow and an abnormally rapid folic-acid plasma clearance test. During the first 22 days of therapy the patient's reticulocyte count reached its peak of 9.6%, her folic-acid plasma clearance test returned to normal and her bone marrow became normoblastic. Her hemoglobin and red cell count rose to normal levels for a premature infant of her age who has not been on supplementary iron. A subsequent increase of dietary and parenteral folic acid to 100 and 200 ug. daily and the administration of ascorbic acid did not result in any further increase in reticulocytes or hemoglobin, indicating that a complete therapeutic response was obtained with the smaller dose of folic acid.

The usual daily dose of 0.4 to 10 mg. of folic acid converts a megaloblastic marrow to normal in 24 to 48 hours. The second marrow aspirate obtained on the seventh day of therapy still showed minimal megaloblastic changes. The delay response in this infant would suggest that the dosage of 50 ug./day of pteroylglutamic acid was close to the minimal therapeutic dose for infants. Although the majority of megaloblastic anemias seen in infants result from folic-acid deficiency, a few are due to vitamin B_{12} deficiency. Whenever the folic-acid plasma clearance test is not available for definitive diagnosis of folic-acid deficiency, we would recommend that not more than 50 ug. of folic acid be administered daily for the therapeutic trial of any suspected folic-acid deficiency in infants. The use of this dosage ought to prevent the masking of a vitamin B_{12} deficient megaloblastic anemia.

Since the daily *minimal requirement of free folic acid* for infants can not exceed the minimal therapeutic dosage, it must be equal to or less than 50 ug./day. Approximately 95% of the dietary folic acid is in the bound or conjugated form,[4,9] and only a minute fraction of this bound folic acid can be converted to free folic acid.[10] Since only free folic acid can be absorbed from the intestinal tract and since the rate of absorption of free folic acid in infants is unknown, the requirements of total (bound and free) folic acid in the diet is unknown.

Summary

A five-month-old premature infant with chronic diarrhea and pneumonia developed megaloblastic anemia due to folic-acid deficiency. Daily therapy with 50 ug. of pteroylglutamic acid converted her magaloblastic bone marrow to normal with a rise of reticulocytes, red cells and hemoglobin. Because the response to therapy was delayed, this dose of 50 ug. is probably in the range of the minimal therapeutic dosage of folic acid.

Since 50 ug. of pteroylglutamic acid administered daily resulted in a complete cure of the infant's megaloblastic anemia, the daily minimal requirement of free folic acid is equal to or less than this amount.

Acknowledgment

We are indebted to Miss Janet Bowne and Mr. Vernon Delgado for performing the hematological determinations.

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Unless the urinary secretion is restored, death usually occurs on about the eighth day. It may, however, be reversible and in those who do survive, there may be a post anuric period of several weeks with impaired function, nitrogen retention and diminished concentration of the urine.

Durham, Robert H. — Encyclopedia of Medical Syndromes.
Hoeber Medical Division,
Harper and Row, New York

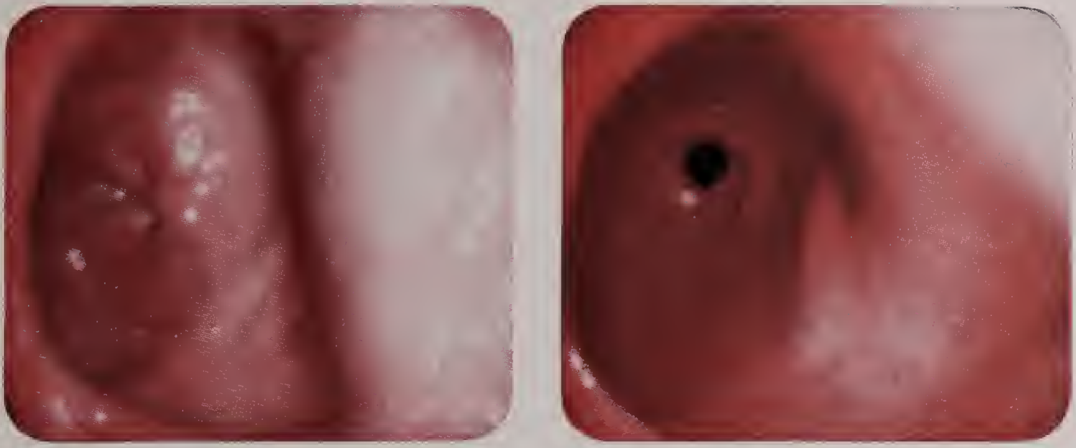
Derivatively Speaking

Ficus: from Latin *ficus,* a fig

If men use their liberty in such a way as to surrender their liberty, are they therefore any less the slaves? — Herbert Spencer, 1851

Mankind are poor, transitory things; one day in life, and the next turned to ashes. Therefore manage this minute wisely and part with it cheerfully; and like a ripe fruit, when you drop, make your acknowledgements to the tree that bore you.

— Marcus Aurelius



Intragastric photography studies[1]

A/ E. B., male, age 48. Normal antral contraction. Pyloric opening is not seen. It is difficult to differentiate a deep prepyloric contraction from a "pyloric fleurette" or true pylorus.

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1. Barowsky, H.; Greene, L., and Bennett, R.: Investigators' Clinical Report. Photographs courtesy of Drs. H. Barowsky, L. Greene and R. Bennett.

2. Barowsky, H.; Greene, L., and Paulo, D.: Paper read at Meeting of American Society for Gastrointestinal Endoscopy, Montreal, Canada, May 25-27, 1965.

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ONLY RARELY do different departments of the same medical faculty contribute as a unit to provide an issue for national publication. Although there are some well-known journals which are products of individual medical centers, most of us contribute to journals within our respective disciplines and for readers in those disciplines. As a result, we all have a tendency to be unaware of current work in progress in other departments within our own medical centers. The opportunity

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to fashion this issue of MINNESOTA MEDICINE has proven highly gratifying to us. The call for ideas and contributions has made us acutely aware of the diversity and caliber of the current work in progress in the clinical departments here. In retrospect, the only painful aspect of the participation has been the necessity for selection of papers because of limitations of space. The contributing editors are grateful that this activity has provided us occasion to browse through some of the work in other medical areas than our own at this Medical Center. We also have come to appreciate to what a degree there is not only a willingness but an eagerness to achieve our ends by competitive and yet congenial effort.

We wish to express our very real appreciation to the Editor-in-Chief of MINNESOTA MEDICINE for his very generous invitation to participate with him in this manner.

Clarence Dennis, M.D.
Marvin L. Gliedman, M.D.
Brooklyn, New York

State University of New York Downstate Medical Center

IN THIS special issue of MINNESOTA MEDICINE I would like to express the pleasure and pride the Downstate Medical Center Faculty and Administration take in the opportunity offered here to report to associates in another part of the country some of the many activities in progress at our rapidly expanding Medical Center in Brooklyn.

We in Brooklyn feel strong ties to our associates in Minnesota. The editors of this special issue — Drs. Clarence Dennis and Marvin Gliedman — both have been associated with the University of Minnesota. Dr. Dennis, who came to Downstate in 1951 as Professor and Chairman of Surgery, was associated with the University of Minnesota for 16 years. He received his M.S. in physiology and his Ph.D. in surgery, took his internship and residency training in surgery there, and served on the faculty for 12 years. Dr. Gliedman, a graduate of Downstate, took his surgical internship at Minnesota and is now a Markle Scholar at State University of New York.

Another department chairman — Dr. Harry Mellins in Radiology — spent four years on the Minnesota faculty. Drs. Karl Karlson, Irving Enquist, and Harry Kaplan, all in the Department of Surgery, are Minnesota medical graduates. Drs. Karlson, Charles Fries, and Irving Enquist, in Surgery, interned at Minnesota; Dr. Karlson also received his Ph.D. there. Many others with Minnesota backgrounds, some of them contributors to this issue, have joined the State University of New York.

On the other side of the picture, we are pleased that a number of our graduates have gone to the University of Minnesota. One of our graduates and interns, Dr. Eugene Bernstein, is now a Markle Scholar with Dr. Owen H. Wangensteen at Minnesota.

Great progress has been made at the Downstate Medical Center since it became part of the State University of New York in 1950. Enrollment in the College of Medicine was 110 students in 1950; this year the first class of 200 was admitted. A Graduate Educational Program to train teachers and researchers in the basic medical sciences was established in 1956 and now has an enrollment of 60. The number of full time faculty members has been more than trebled. Affiliations with community hospitals have been increased and fortified. A new Basic Sciences Building was opened in 1956 providing modern facilities for research and teaching in the six basic sciences. This year two new residence halls for students and their families were opened next to the Basic Sciences Building.

Meanwhile, construction is advancing on a new University Hospital, scheduled to open in 1966. This building is connected to the Basic Sciences Building by a clinical sciences wing. The Hospital will have 350 beds and facilities for 110,000 outpatient visits a year, as well as facilities for research in the clin-

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6206

ical departments, which will adjoin each department's nursing unit. Plans for the future include a College of Nursing to be opened in conjunction with the Hospital, and eventually a College of Health Related Services. Curricula in occupational and physical therapy, to be part of the latter College, will begin in the fall of 1965. The Medical Center Library has been merged with the Library of the Academy of Medicine of Brooklyn, one of the largest medical libraries in the country, and the entire collection will be housed in the Basic Sciences Building at Downstate.

As the only Medical school in Brooklyn and Long Island — an area with approximately 7,000 physicians and a population of four and half million — the Downstate Medical Center is becoming a center for meetings and educational activities of professional organizations and hospitals and the focal point and coordinating agency for postgraduate courses and scientific symposia and conferences in the area. Many medical organizations now hold their regular meetings at Downstate. Furthermore, the Center, in cooperation with the Kings County Medical Society and other medical organizations, offers a varied program of postgraduate courses throughout the academic year. The Medical Center and the various departments are also increasingly acting as host to medical and scientific organizations, groups, and individuals from other parts of the country and the world. Visitors are cordially welcome at Downstate and we hope that this special issue will encourage many of our Minnesota colleagues to pay us a visit.

Robert A. Moore, M.D.*
Brooklyn, New York

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*President of the Downstate Medical Center of the State University of New York and Dean of the College of Medicine.

Annotation on Life

THE EMOTIONAL argument for therapeutic abortion was recently dramatized in Life Magazine, June 4, 1965. The threat of congenital malformations occurring in the fetuses of mothers infected with rubella virus early in pregnancy has seldom been so poignantly illustrated. Anticipation of the major epidemic of congenital malformations which will follow the present rubella epidemic has caused many persons to question the 20th century validity of 19th century laws on therapeutic abortions.

The plight of mothers carrying deformed fetuses was newsworthy during the Thalidomide scare but, because of Dr. Frances O. Kelsey's careful work, had minimal emotional connotation for the American people. The present rubella epidemic, however, provides an emotional as well as a real threat, for few pregnant women are absolutely sure that they have not had rubella and can be completely isolated from contact with children who have the disease.

The pregnant woman who is aware of the threat realizes that she has a substantial chance to have a deformed infant if she acquires clinical rubella. She may not know that exposure alone, without clinically evident rubella, carries a significant risk. On the other hand, as several other viruses can produce a clinical picture and skin rash which closely resemble rubella, she may be falsely alarmed by a mild fever and skin rash. A new complement fixation test, developed at the National Institutes of Health and available at the U. S. Communicable Disease Center in Atlanta at the request of state health departments, will tell within 24 hours whether or not a person has had a recent rubella infection. If the test is negative, uncertainty will be resolved for the pregnant mother, but if the test proves recent rubella infection, uncertainty, doubt and probably fear will be established.

She will be concerned about what could happen to her child. Any of the following anomalies could occur: auditory sac absence

Continued

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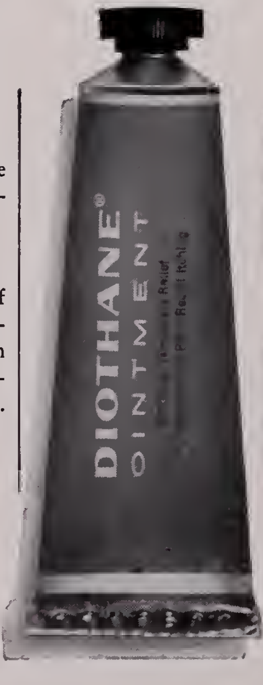

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The pregnant woman will be concerned about the likelihood of something happening to her child. The incidence of malformations after rubella infection is not constant; it depends upon the time in pregnancy when the infection occurs, and it decreases with the duration of pregnancy. Retrospective studies, correlating rubella infection with malformations, disclosed that between two and four weeks after the last menstrual period almost 60% of fetuses were deformed, between five and eight weeks about 35%, between nine and 12 weeks about 15%, and between 13 and 16 weeks about 7%. The over-all risk for the first 16 weeks was 21%. The risk during the first two weeks of pregnancy was undetermined; it may have been higher or lower than 60%. The risk after 16 weeks (also unknown) may have become very small. These figures have a corollary value and a positive side: the chances of a child not being affected when the mother has rubella increases with duration of pregnancy. These chances appear to be about 40% if the infection occurs between two and four weeks after the last menstrual period, 65% between five and eight weeks, 85% between nine and 12 weeks and 93% between 13 and 16 weeks.

At a recent symposium on rubella infections held in Philadelphia,[2] a report of a prospective study after proven rubella infection indicated an over-all risk of congenital malformation for the first trimester to be about 19%. This study found in the first four weeks a risk of 47%; from five to eight weeks a risk of 22%; and from nine to 12 weeks a risk of 7%. Another preliminary report at this symposium suggested that gamma-globulin prophylaxis, after known exposure to rubella, may decrease the incidence of both clinical and subclinical rubella infections and, therefore, the incidence of malformations. Well controlled studies of this treatment are needed before it can be recommended. Such studies on the natural history of maternal and fetal rubella, on prophylaxis and the development of new tests for diagnosis will do much to remove the uncertainties about past and present infection and will clarify the prognosis for the infant. Since the most critical period for the fetus is in the early weeks of pregnancy before the mother seeks medical care, perhaps even before she knows that she is pregnant, the ultimate answer will be the development of an effective rubella vaccine which can be given to all children with booster doses for married women. Until these problems are solved the issue of the pregnancy complicated by rubella remains urgent.

Maternal rubella infections also cause an increased rate of spontaneous abortion. Physicians have long assumed that spontaneous abortion is the result of a natural-process selection. The evidence so far accumulated supports the assumption that spontaneous abortions are usually associated with gross congenital deformities, major deformities incompatible with life, or chromosomal aberrations. We infer, therefore, that spontaneous abortion is not a pathologic process, but an efficient, beneficial and necessary process by which defective fetuses are eliminated.

If spontaneous abortion is the natural process by which deformed fetuses are rejected, and if the observed increased incidence of spontaneous abortion after rubella infection is compatible with this hypothesis, then the process functions inadequately, for many deformed infants are not rejected *in utero*. Surgical intervention is frequently indicated when other body functions fail. Therapeutic abortion is often sought by pregnant

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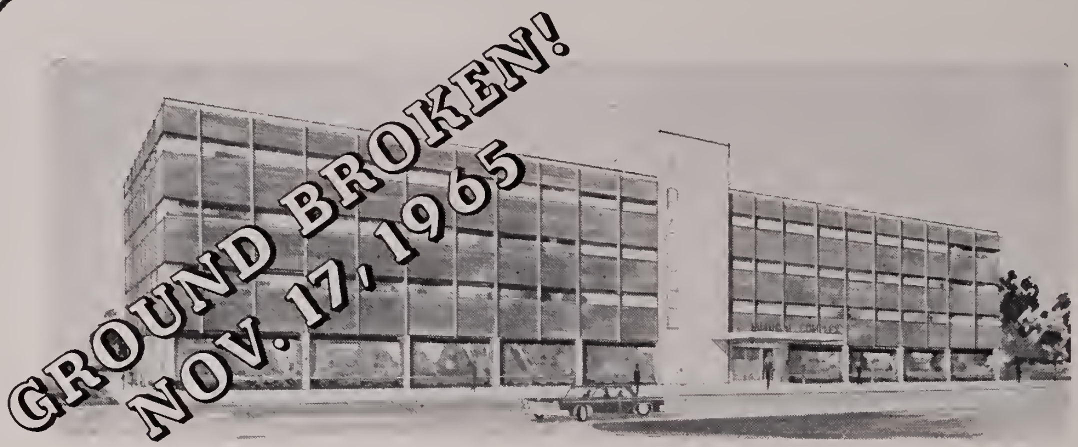
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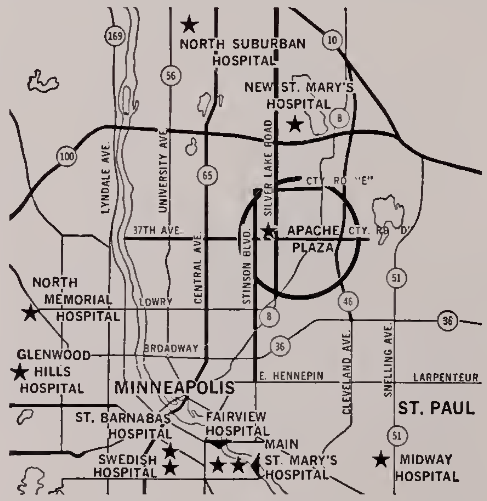
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women who have maternal rubella and do not have a spontaneous abortion. The surgeon who intervenes when other normal processes fail may on this basis find justification for therapeutic abortion, even though there is a good chance that the fetus may be normal. The analogy to the removal of a normal appendix after operation for suspected appendicitis is inadequate, though common enough to offer a parallel.

This suggestion that therapeutic abortion may be a remedy for a suspected malfunction of the normal process of spontaneous abortion is not offered as an excuse for the indiscriminate use of the curette. It is offered as a justification for such last resort treatment when careful consideration by both parents and physician has been given to the diagnosis of rubella, the stage of pregnancy, the likelihood of deformity and normality in the fetus, and the danger of the operation.

If the concept that a natural process of selection is active in determining the fate of a conceptus by balancing its metabolism and physiology in some yet unknown way to tell if it is normal or abnormal and then preserving the nidation* or initialing abortion, the natural law argument that pregnancy alone is normal is nullified. Then the ethical considerations for termination of pregnancy when fetal congenital malformations are suspected become personal matters to be decided by the parents and the physician.

If faced with this problem, the parents and the physician should consider carefully all the scientific facts available as well as the intangible doubts and dreads, and without hesitancy seek the counsel and advice, but not the dictate of minister, priest or other physicians. As yet, the legal justification for therapeutic abortion for suspected congenital malformation in a fetus does not exist in most states; but personal observations and historic precedent indicate that medical practice is usually in advance of both clerical and legal reform.

Warren J. Warwick, M.D.
Minneapolis, Minnesota

See Test Your Word Score Below.

References

1. Rendle-Short, J.: Maternal Rubella. Lancet 373, 1964.
2. Rubella Damage to Infants Held to Involve Most Organs of Body. Pediatric Herald 6:5, 1965.

Test Your Word Score

Watch for the asterisks in the manuscripts each month and test your word sense!

Heterograft — *taken from an animal* (page 1605).

Hypertelorism — *abnormal distance between two paired organs* (page 1613).

Osmolality — *the number of osmoles of a solute per kilogram of solvent* (page 1616).

Nidation — *the embedding of the early embryo in the uterine mucosa leading to pregnancy* (page 1639).

Exenteration — *evisceration* (page 1654).

Cognitive — *having the faculty of knowing* (page 1659).

Agnosia — *lack of sensory ability to recognize objects* (page 1660).

Homogenates — *tissue ground into creamy consistency — the cell structure disintegrated* (page 1697).

Pathogenesis — *the mode of origin of a disease* (page 1701).

Idiopathic — *a high-flown term to conceal ignorance* (page 1719).

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Letter to the Editor:

Pertaining to your Toonerville remarks, I am distressed to hear that you think that we who live in small towns do not practice up-to-date medicine. I can assure you that we do. — M.D.

Editor's note: See Soliloquy below.

The Editor's Soliloquy

Toonerville*

I quess I "goofed," was misunderstood, and I feel badly! I apologize! There are no longer any doctors in Toonerville. They all moved out. In Grandfather's day I was raised in a Toonerville, where the only evidence of modernity was a postoffice and a whistle stop on a branch line of the Milwaukee Railroad. There were endless prairies, sky and sunshine, with the closest neighbor miles away.

In my teenage mind — though our Toonerville was a single street with a dust-covered road leading to the swimming hole, and with more than enough territory for any man to roam, to fish in the creek, or to enjoy nature — I wondered why anyone would want to move to a larger metropolitan area, only to succumb to the 'rat race.'

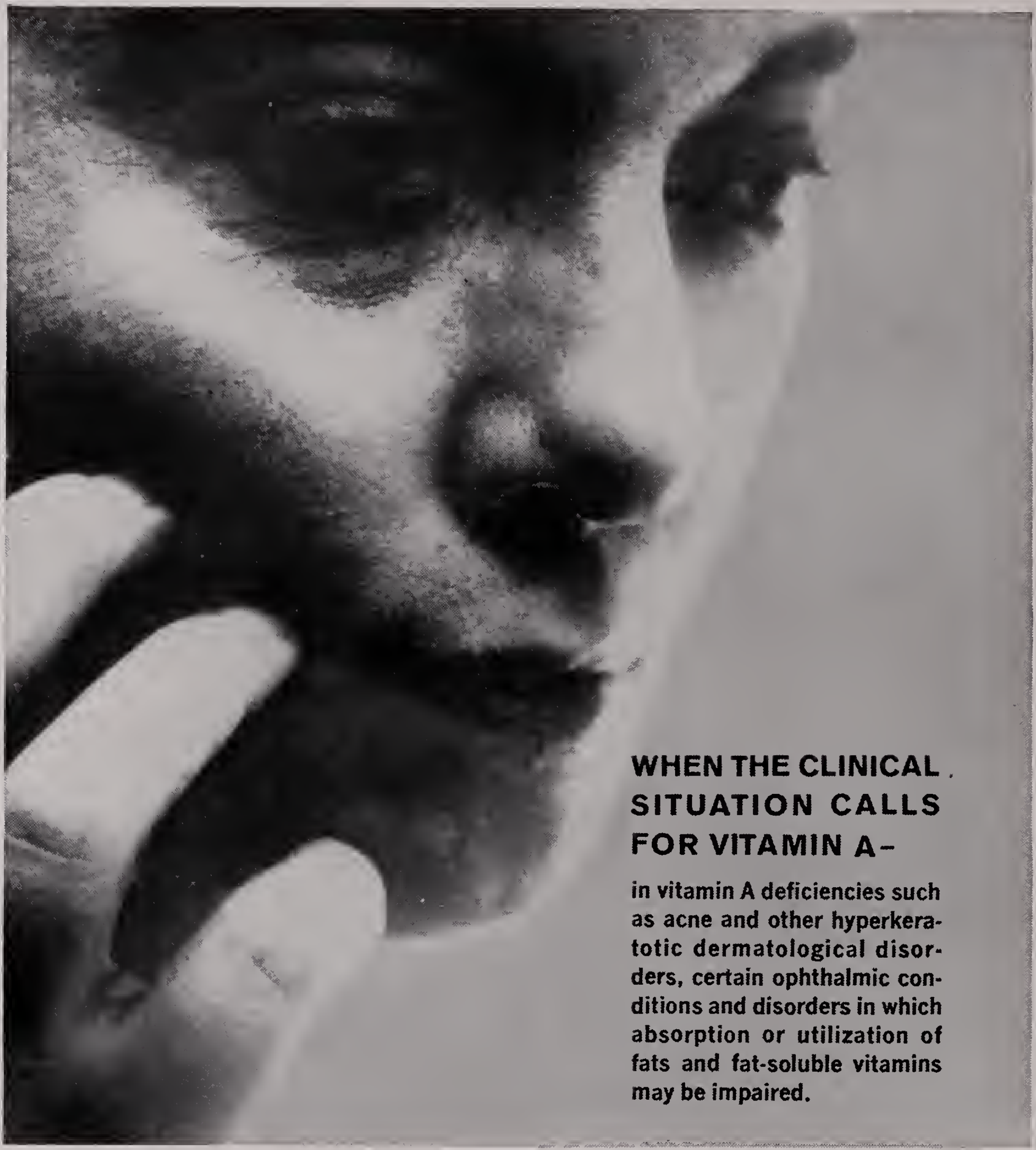
In those horse-and-buggy days our doctor conducted a thriving practice from the hair-cushioned seat of his one-horse surrey. Many a time I rode with him on his daily rounds out into the Dakota hills, with the privilege of holding the reins while he compounded aromatic medicines, perused a magazine with strange and incomprehensible drawings, or occasionally took a snooze as he relied upon me to deliver him to the home of the next sick Indian.

By the time I had finished high school the doctor had moved from our Toonerville; and ever since then a half dozen local families here and there, abetted by the government, have tried to persuade doctors to move back to the Toonervilles all over the country. But only if our republic is taken over by a dictator or surrenders to a dynasty, will we physicians consent to practice medicine under such benighted or debased conditions.

The small towns in our nation, now with ready access to hospitals and medical facilities, are the most rewarding places to live. For gratifying interpersonal relationships they have no peers. They cherish rich traditions and foster cultural and intellectual pursuits on a par with those maintained in any large metropolitan center. These smaller towns are the heart of our society; they are the communities in which a physician can live a full life and serve humanity capably and devotedly, as he had originally planned to do when he took up the study of medicine.

Though some small towns do not have as many physicians as they could accommodate, it is not these small towns to which the government wants us to move. It wants us to move to the Toonervilles, the towns that cannot support a modern medical practice: the towns with a postoffice and a whistle stop and endless miles of nothing, where no doctor could practice good medicine even from a down-cushioned seat in his automobile.

Carl O. Rice, M.D.



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ANSWER: The majority of patients need but a single bronchoscopy, granted they stop smoking. Generally speaking, if very little emphysema is present, the outlook is an excellent one. On the other hand, if the patient already has severe emphysema, his chances of getting into difficulty are far greater, and subsequent bronchoscopies may be needed when the patient runs into difficulties, particularly with exacerbations of respiratory infection. Thus it can be said that the duration of the good result from the treatment outlined varies inversely with the severity of the disease.

David H. Waterman, M.D. for
Drs. Waterman, Domm and Rogers,
Knoxville, Tennessee

Isoniazid and Para-Aminosalicylic Acid

QUESTION: Would you recommend the use of steroid therapy in conjunction with isoniazid and para-aminosalicylic acid in the management of a case of primary tuberculosis? The patient is a six-year-old child with enlarged bronchopulmonary lymph nodes which have resulted in segmental collapse of the right upper lobe. She has been under treatment with isoniazid and para-aminosalicylic acid for four months without roentgenographic evidence of clearing of the chest problems.

ANSWER: Drugs such as prednisone and triamcinolone combined with anti-tuberculous chemotherapy have been tried in such cases, but the evidence does not indicate that it is of substantial benefit. If a favorable response results, it is generally felt to occur in those cases in which steroids are utilized early in the course of the disease — within the first three months of the illness. Therefore, I would not advise the use of steroids in the case under question. Management of these difficult cases is best shared with a qualified medical-surgical chest team.

Harold D. Kletschka, M.D.
State University of New York
Syracuse, New York

The desire to take medicine is perhaps the greatest feature which distinguishes man from animals. — William Osler

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Fracture–Trauma Conference

Replantation of Limbs

Dr. Gerald Shaftan*

This morning we are presenting a conference on a subject that has fascinated surgeons since antiquity — the replantation of amputated limbs. Our guest is Dr. Ronald A. Malt from the Surgical Services of the Massachusetts General Hospital and the Shriners Burns Institute, Harvard Medical School. Dr. Malt, an Established Investigator of the American Heart Association, three years ago reattached the amputated arm of a young boy. This probably was the first successful replantation. The following are the case reports of our own replantations.

Case Reports

Case No. 1

On November 10, 1962, a 52-year-old printer caught his hand in a rotary printing press. The hand was pulled off at the carpal-radial junction and was spun around and crushed in the press before being removed. The patient and the hand were brought to the hospital immediately, and while the patient was being resuscitated, the hand was washed, placed in a penicillin solution and refrigerated. It was then perfused at operation 90 minutes later. The carpus was transfixed with Kirschner wires and the radial artery anastomosed, using 6-0 silk. A single vein was repaired on the dorsum of the hand and ulnar artery continuity was restored with a saphenous vein graft. By this time the radial artery anastomosis had thrombosed and was taken down and redone. Postoperatively, capillary filling was noted for a period of 24 hours; but the hand then became obviously nonviable and was amputated on the fifth postoperative day.

Case No. 2

On November 22, 1962, during a store robbery, a 31-year-old male clerk had his left hand transected through the carpus with a meat cleaver. He was brought to the hospital with a policeman's night stick as an upper arm tourniquet controlling the hemorrhage and the hand dangling from the wrist by a 2-cm. bridge of volar skin. A catheter was immediately inserted into the radial artery and the hand was perfused with low molecular weight dextran in saline to which heparin had been added. After clearing the distal arterial tree, the radial and ulnar arteries were repaired, the carpal bones were fixed with heavy Kirschner wires to the radius, and four venous anastomoses were made on the dorsal and lateral surfaces of the wrist. The order of repair was dictated, in this instance, by the desire to preserve the bridge of intact volar skin.

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*Associate Professor of Surgery, State University of New York.

Continued

Low molecular weight dextran was continued on the first postoperative day, after which systemic heparinization was given for four more days. There was minimal postreplantation edema. Intraosseous venograms on the fifteenth postoperative day demonstrated at least two intact venous channels, and arteriography one week later showed good flow in the radial and ulnar arteries. Subsequently the median and ulnar nerves and flexor and extensor tendons were repaired, and an opposition bone blocking of the thumb-index metacarpals was done. This has produced a functional hand with good sensation to touch, temperature and pin prick, although two-point discrimination is limited to 20-30 mm. at the finger tips. He has the ability to hold a glass and other large objects and has sufficient facility to strike matches. He has returned to work.

Case No. 3

In July 1964, a 28-year-old man apparently slipped under a subway train, crush-amputating his right upper extremity. On admission to the emergency room the few shreds of tendon attaching the arm to the body were divided so that a separate team was able to begin the perfusion and cooling of the arm through a catheter in the brachial artery. Again, low molecular weight dextran and heparin were infused until the perfusate returning from the veins was clear. The arm was placed in a bucket of iced saline and brought to the operating room with the resuscitated patient. The brachial artery was anastomosed first, and immediate perfusion of the arm was permitted with free venous back-bleeding. This enabled us to identify two major veins which were repaired prior to the stabilization of the humerus with a Rush pin. Infusion of low molecular weight dextran was continued postoperatively and apparently caused a good deal of bleeding, for within five hours after completion of replantation, the patient was returned to the operating room for ligation of numerous small arterial and venous bleeders in the distal stump musculature. Edema and bleb formation increased rapidly up to the third postoperative day, then gradually subsided. Five months later the Rush pin was removed, the humerus shortened two inches and fixed with an A-O plate, permitting good skin coverage. At the present time the patient is awaiting nerve repair; however, the tag approximation of the nerves done at the initial procedure has enabled some regeneration of nerve fibers. The patient has sensation around the elbow and on the radial border of the forearm and is able to contract his biceps muscle.

Case No. 4

In August 1964, a 15-year-old boy had his hand severed at the wrist by a sabre during a fight. The amputation was between the distal and proximal row of carpal bones. The hand had been transported in ice and was perfused as in the two preceding patients. The carpus was first transfixed with Kirschner wires, the radial and ulnar arteries were then anastomosed, and four veins on the dorsal and ventral surface were also repaired. The result was encouraging and good nail bed perfusion continued for four days. On the fifth postoperative day blebs began to form and some cyanosis was noted in the nail beds. The patient had been continued on low molecular weight dextran, 1,000 ml. per day, and subcutaneous bleeding had occurred at the amputation site. Removal of the clots under the skin was accomplished in the operating room, which relieved the occlusion of venous return; nevertheless, loss of fingertip viability progressed. At the eleventh postoperative day there was still some hope of salvaging the remaining phalanges and hand, but the necrosis slowly advanced proximally, and the hand was amputated on the twenty-fifth day.

Dr. Ronald Malt*

The group of cases that you have seen and some others like them certainly prove that there is no longer any question about the feasibility of replantation or much doubt about the functional benefits that can be realized for some patients. The real unsolved question is how to select those patients who are going to have enough return of function to make replantation worthwhile both from a personal and from an economic point of view. As far as the technic goes, it is really very simple and can be put down in recipe form.

Immobilize the Bone

First, one obviously has to resuscitate the patient. I feel a little embarrassed even to mention this among surgeons, but sometimes there is the same emotional reaction in the profession to the possibility of a replantation that is seen so often in the nonmedical public. We may completely lose sight of ordinary surgical principles when faced with this very dramatic procedure. Second, and perhaps simultaneously, the amputated part should be cooled. This may be done by putting it in a pail of iced saline or lactated Ringer's solution. Next, flush the arterial system with lactated Ringer's until the perfusate comes back clear, and then clean a little bit of dirt out of the wound; however, at this stage don't make a significant attempt at debridement. In the restoration itself the bone should be attached first. Shortening or reshaping the contour of the bone will increase the stability and the technical facility of repairing structures and resecting questionably damaged areas.

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*Instructor in Surgery, Harvard Medical School, and Assistant Surgeon, Massachusetts General Hospital.

Repair Veins First

We firmly believe that the veins should be repaired before the arteries: first, because of the necessity with preliminary arterial repair for replacement of massive unchanneled blood loss, and second, because occlusion of the veins after arterial continuity is established produces venous hypertension and additional muscular damage.

Debridement

The arterial anastomoses being completed, perfusion of the arm then gives good indication of what needs to be debrided. Debridement must be thorough. Almost every unsuccessful replantation that I have seen failed because the surgeon was reluctant to remove dead tissue. After debridement, nerve ends may be joined for later identification, or perhaps primary repair is indicated in sharp transections more distally in the arm. Finally, the soft tissues are closed and the skin repaired, using available local material, split thickness graft if suitable bed is available, or pedicle flaps if necessary.

We do not use any anticoagulant or low molecular weight dextran in the postoperative period, because it is our feeling that platelet thrombosis is what dooms the arterial and venous reconstruction, and this is not prevented by anticoagulants. Furthermore, on the basis once again of replantations that have failed, many were unsuccessful because bleeding in the postoperative period either jeopardized the patient's life or produced hematomas that subsequently became infected.

Evaluation of the Subject

The conscientious surgeon must weigh evidence on three additional questions before he makes a decision to replant a limb.

Will replantation endanger the patient's life? The immediate hazard is that occult bleeding, a ruptured organ, or a catastrophe such as cerebral herniation may kill the anesthetized patient during replantation. Acidosis from the release of accumulated metabolites immediately after circulation is restored and hypotension from sequestration of plasma within the limb later may also complicate surgical management in the postoperative period. This is especially true if the amputation is many hours old and if the problems are not foreseen in time to be corrected. In the postoperative

Continued

period hemolysis and myolysis are less well treated; they are better prevented by not replanting the badly crushed or autolyzed extremity and by providing for venous drainage before arterial inflow is returned.

Clostridial gangrene and other infections may be lethal at any time, particularly after the cessation of antibiotic therapy. Sporulating organisms may persist in tissue for years until the proper anaerobic conditions for their growth occur.

What are the chances for recovery of function? The standard for comparison is first, the prosthesis. If a good appliance is available and if the amputation is so located that chances of nerve regeneration are poor, for instance below the knee, replantation hardly seems warranted today. In the upper arm, where a better prosthesis can be fitted the longer the stump, a case can be made for replantation to achieve a little more length even if the distal parts are beyond repair.

The condition of the nerves is next considered. Nerves cleanly severed by a sharp instrument and amenable to primary union naturally make the surgeon optimistic. In a recent crushing injury in which a hand was completely devascularized distal to the metacarpal heads, repair of the arterial palmar arch and of the venous drainage were not difficult tasks, but the grossly intact nerves never became capable of transmitting sensation, and the hand was useless.

A sensate hand is, indeed, better than a metal hook. The question is whether functionless feeling is of enough benefit for one particular patient to subject him to the ordeal that follows replantation.

What will replantation mean to the patient? In the best possible situation it will mean that part of a dominant upper limb with minimal injury away from the level of transection will ultimately be restored in every important way to a responsible person. In the worst, it will mean that an extremity of limited utility will be preserved for someone already incapacitated in body or mind at the economic cost of many hospitalizations and at the social cost of psychic invalidism and narcotic addiction.

Nevertheless, only when the surgeon is satisfied by every means available that the patient would be better off with an attempt at replantation than with revision of the amputation, is he justified in restoring a lost limb. The decision to perform an elective operation in an emergency is always more taxing than defining a course of action when life is at stake.

Dr. Shaftan

Thank you, Dr. Malt. I can see that a number of questions have already been answered by your illuminating discussion, but there is some difference of opinion on some points. In our last three cases, clearing of the microcirculation with a mixture of low molecular weight dextran and heparin was utilized. You apparently don't make any attempt to do this immediately.

Dr. Malt

No, but we do perfuse subsequently. My guiding philosophy in most surgery is to keep it as simple as possible and in general I am against using two teams. I would rather wait until I am absolutely certain that things are going to be O.K. before I perfuse the limb. Shorey's[1] experimental studies in Chicago compared low molecular weight dextran, heparinized saline and other perfusates for their effectiveness in clearing microcirculation in an amputated part. They found that heparinized saline was more effective than low molecular weight dextran, although I must say that intellectually my sympathies are with low molecular weight dextran.

Dr. Horace Herbsman*

The same study did show that low molecular weight dextran perfusion produced the least limb edema. While we combined low molecular weight dextran and heparin, which may be the ideal perfusate, we got edema in the last two cases. We feel that the adequacy of the venous anastomoses is more important in preventing edema than lymphatic regrowth or the type of perfusate.

Dr. Shaftan

Turning to the problem of the order of repair, we have preferred to anastomose the arterial supply first, permitting earlier oxygenation of the extremity. Free bleeding from the veins has facilitated venous repair, especially in the small veins of the wrist and hand.

Dr. Malt

With cooling of the extremity there is no great hurry to restore circulation rapidly; moreover, it isn't exceedingly time-consuming to do venous and arterial repairs. I don't see that we should lose more blood than necessary.

Dr. Herbsman

Perhaps in the upper arm or leg, venous loss would be so great as to be prohibitive, but certainly in the more distal transections we lost relatively little blood and were able to find veins for repair that were impossible to locate before arterial flow was established.

Dr. Shaftan

Dr. Herbsman has mentioned that we feel that adequacy of venous return is a paramount factor in preventing edema. How many arterial and venous anastomoses do you think are necessary?

Dr. Malt

Don't you think that you ought to do as many as you can — within reason? In the upper arm one artery and one vein will do. In the hand one should try to repair the radial and ulnar arteries and two or three veins. We connected only one vein in the arm, and I know of at least two other replantations in which only one vein was connected without subsequent significant edema. We should try to do the tendon repairs at the primary operation. If everything else is *perfect* it would also be advantageous to repair the nerves.

Dr. Herbsman

We feel that repair of more than vessels and bone at the time of replantation adds unnecessarily to the procedure when the survival of the extremity is still not assured.

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*Instructor in Surgery, State University of New York.

Continued

Dr. Joseph Tuby

If the limb is not brought with the patient, what is the time limit after which it should not be replanted? If you cool the limb while resuscitating the patient, does that change your time limit?

Dr. Malt

Several bits of experimental evidence bear on that, but clinical evidence suggests that you can get limb recovery up to six hours at room temperature. While definitive studies have not been done, Nabseth's[2] work suggests that you can probably get survival within 18 hours if a limb is cooled.

Dr. Herbsman

Lapchinsky[3] in Russia successfully autotransplanted canine limbs preserved for as long as 28 hours at 2°-4° C., with full return of muscle and nerve function.

Dr. Marvin Gliedman

How many tries have been successful?

Dr. Malt

I know of about 36 replantations; we have had two. By definition all replantations are of complete severances. Approximately 12 to 15 have results that I think would please the patient.

Dr. Shaftan

Thank you, Dr. Malt, for coming down to participate in this conference. I hope it stimulates prudence as well as interest in attempting replantation of amputated extremities.

Gerald W. Shaftan, M.D.*
Horace Herbsman, M.D.**
Ronald A. Malt, M.D.†
Brooklyn, New York

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Anglo Saxon Leech Craft

If the shanks be broken, take bonewort, pound it, pour the white of an egg out, mingle these together for the man whose shanks are broken. For a broken limb, lay this salve on the broken limb, and overlay with elm-rind, apply a splint; again, always renew these till the limb be healed. Clean some elm-rind, and boil it thoroughly, then remove the rind, take ground linseed and brew it up with the drink of elm. That shall be a good salve for a broken limb.

— Payne, J. F.; English Medicine in Anglo Saxon Times,
Oxford at Clarendon Press, 1904.

"So plan as though you'd live to be 100; so live as if you might die tomorrow."
— E. O.

Tumor Conference

Malignancy of the Female Genitalia

The Status of Radical Surgery in the Treatment

The history of surgery as treatment for malignant lesions of the female genitalia is a long and familiar one. Since Wertheim[1] first described his surgical approach to cervical carcinoma there has been an emotional reaction to the mere mention of radical pelvic surgery among physicians. These reactions have resulted in periods of popularity for radical surgery alternating with periods during which radical surgery was almost dropped from the armamentarium. The present period might be called one of popularity for such surgery and dates from Meigs' first case in 1939, or more substantially from his first report in 1944.[2] This adoption and subsequent rejection of the use of radical pelvic surgery was implemented by the constant striving to improve the results of treatment. Radical surgery was displaced when radium became available, and this period was prolonged by the development of x-ray treatment.

World War II accelerated the return of radical surgery by virtue of stimulating the development of anesthesia, antibiotics and blood banks. This great interest in surgery over the last 25 years has, no doubt, acted as a stimulus to radiologists to improve their methods as well as their results. Supravoltage therapy has evolved during this period and has brought both improvement in results and new complications. Another development during this period has been improved communication throughout the world. At the same time standardized methods of reporting have been adopted, leading to the full realization that neither surgery nor radiation alone can achieve maximum benefit for patients with pelvic malignancy. Table 1 demonstrates the fact that the majority of cases of carcinoma of the cervix as of 1958 were still in advanced stages when detected. This means, as shown in Tables 2 and 3, that approximately one out of every two cases seen and treated will result in failure, not to mention the complications of treatment that will occur. If radiation fails in a case of early Stage II carcinoma of the cervix the only hope left for

Continued

that patient is radical surgery. In the most optimistic clinic in the world radiation will fail in one out of four cases of Stage II carcinoma of the cervix, while in practically all clinics of the world the failure rate in Stage II is approximately 50 per cent.[3] Thus we have entered a new period in the history of radical pelvic surgery, namely, one in which its place is secure and equal to that of radiation therapy. It seems fitting to spell out this status of radical surgery.

TABLE I
Carcinoma of the Cervix 1948-1957 Inclusive
Number of Patients Treated

		Stage I		Stage II		Stage III		Stage IV	
Institution	Total No. Treated Cases Stages I-IV	No. of Cases	%	No. of Cases	%	No. of Cases	%	No. of Cases	%
Graz, Austria	1,930	545	28.2	770	39.9	524	27.2	91	4.7
Vienna	843	261	31.0	210	24.9	337	40.0	35	4.1
Copenhagen	3,109	1091	35.1	988	31.8	786	25.3	244	7.8
Munich	4,910	771	15.7	1675	34.1	2292	46.7	172	3.5
Calcutta	1,593	207	13.0	332	20.8	987	62.0	67	4.2
Stockholm	3,833	673	17.6	2094	54.6	807	21.0	259	6.8
Manchester	3,410	348	10.2	1759	51.6	978	28.7	325	9.5
Houston	1,155	165	14.3	491	42.5	448	38.8	51	4.4
N. Y. Col. Presb.	580	234	40.3	206	35.5	102	17.6	38	6.6

Ovarian and Endometrial Carcinoma

In such a discussion it is logical to consider the problem from the standpoint of primary cancer sites. Ovarian carcinoma can quickly be dismissed from the discussion as there is no place in the treatment of this disease for radical operations. Total abdominal hysterectomy with bilateral salpingo-oophorectomy constitutes the treatment of choice for malignant ovarian lesions. As the lymphatic drainage of the ovaries is primarily to the para-aortic nodes, lymphadenectomy is illogical. The typical intraperitoneal spread of ovarian carcinoma similarly makes radical removal of the pelvic organs useless.

In the case of endometrial carcinoma much the same conclusions have been reached, namely, that radical pelvic surgery is of no value, a not-so-obvious fact that had to be demonstrated by actual clinical trials.

Carcinoma of the Cervix

Cervical carcinoma spreads primarily to pelvic structures which can be encompassed by radical operations, a fact which has led to the development of the surgery under discussion, and it is the most common pelvic malignancy, making up 50 to 55 per cent of all gynecologic malignancies. It is the second most common malignancy in the female.

Contraindications for Radical Surgery

There is wide general agreement that radical pelvic surgery should not be employed as a palliative measure. If, at the time of surgery, spread to para-aortic lymph nodes or other upper abdominal structures is found, then the case should be considered nonresectable and closed.

It has been found that radical radiation and radical surgery, when combined for primary therapy, add significantly to the morbidity and mortality resulting from either alone but do not significantly raise the survival rates.

Radical surgery is, by definition, inadequate therapy for Stage III carcinoma of the cervix and doomed to fail, since the disease has already reached the lateral pelvic wall. In Stage IV carcinoma of the cervix radical surgery is generally contraindicated. There is an occasional case with anterior or posterior extension but little or no lateral spread. In such Stage IV cases radical surgery can be employed; however, there is little enthusiasm for its use anywhere in the world. Thus, the use of radical surgery in the treatment of cervical carcinoma is limited to Stages I and II, as well as to recurrent cases.

Radiation and Radical Hysterectomy

Stage I lesions of the cervix lend themselves well to either radiation or radical hysterectomy. The five-year survival rates as shown in Table 2 range from 70 to 90 per cent; however, the differences in survival rates are probably not as great as those figures suggest. In order to assess this more meaningfully it is important to know the proportion of microinvasive cases included in a given series. This was well illustrated by Latour,[4] who demonstrated a 95.4 per cent survival in microinvasive cases or Stage I A, as opposed to a 73.1 per cent five-year survival rate in Stage I B or clinically apparent Stage I cases. Thus it seems reasonable to equate the results achieved with radiation and radical hysterectomy in Stage I carcinoma, at least until more detailed analyses are available. Radical hysterectomy seems the more desirable method in cases of Stage I A because it is less apt to interfere with vaginal function; furthermore, such patients are usually quite young.

Brunschwig[5] reported an unselected group of cases of cervical carcinoma treated by radical surgery; Masterson[6] reported an unselected group of Stage I cases treated by radical hysterectomy. In both instances the purpose was to assess the role of radical surgery without selection of cases. Where serious medical problems are encountered which make the patient a poor operative risk, radiation therapy can be used with less danger to the patient.

TABLE 2
Carcinoma of the Cervix, Evaluation of Results 1953-1957

		Stage I		Stage II		Stage III		Stage IV	
Institution	Total No. of Cases	No. Treated	% Alive 5 Years	No. Treated	% Alive 5 Years	No. Treated	% Alive 5 Years	No. Treated	% Alive 5 Years
Graz, Austria	889	284	80.6	350	51.4	206	14.1	49	6.1
Vienna	481	167	90.4	102	55.9	194	28.9	18	0.0
Copenhagen	1567	497	71.6	577	53.2	400	25.0	93	5.4
Munich	2424	376	81.4	971	68.7	992	44.2	85	8.2
Calcutta	940	109	61.5	172	30.2	636	14.5	23	4.3
Stockholm	2056	386	87.6	1139	58.2	405	26.9	126	7.9
Manchester	1760	252	68.7	985	45.8	394	27.2	129	7.8
Houston	789	110	92.7	309	76.1	334	46.1	36	22.2
N. Y. Col. Presb.	343	136	73.5	130	43.1	53	18.9	24	0.0

The Risk of Fistula

Many will quickly point out that there is an increased risk in radical pelvic surgery from fistula formation; but it now seems possible to reduce this complication to a level comparable to that with radiation therapy.

Continued

Antoine, Louros, and Debiasi[7-9] have reported fistula rates of 1 to 2 per cent, in marked contrast to the usual figure of 8 to 10 per cent. As Masterson[6] pointed out, the high fistula rate after radical hysterectomy is usually found in clinics where physicians are being trained to do this type of surgery. It should also be pointed out that the control of radiation therapy has been less rigorous in the past than has control of operative procedures. In many cases follow-up after radiation therapy has been poor and radiologists' knowledge of their own results somewhat sketchy. In contrast to this, radical pelvic surgery has been almost entirely limited to centers or to private hospitals with surgeons operating as consultants from centers. Briefly then, it seems reasonable to equate the over-all results of radiation and surgery in the treatment of early carcinoma of the cervix. The results of these two modalities when compared in the treatment of late carcinoma of the cervix might also be equated in terms of 5-year survival rates. A comparison, however, in complications rates would demonstrate an unequivocal superiority of radiation therapy.

Recurrence

As noted previously some 10 to 30 per cent of Stage I cases of carcinoma of the cervix and approximately 40 to 50 per cent of Stage II cases treated by radiation therapy will prove to be persistent or recurrent, a fact that led to the development of more radical surgical procedures. In large clinics today with active and well organized follow-up procedures all cases of cervical carcinoma are carefully followed for evidence of persistent disease or early recurrence. This is most important during the first two years following treatment, when recurrence is most apt to occur. If one can detect recurrence of a Stage I or II carcinoma of the cervix in its early phases, it may be possible to eliminate the disease by a radical hysterectomy. This concept is important because the problem involves a great many patients, and very young patients for the most part. If recurrence is detected in later phases, then it may be necessary to carry out an exenteration* to encompass the lesion.

Modalities of Therapy

Whether one does an anterior, a posterior, or a total exenteration depends, of course, on the location and extent of the lesion. Brunschwig[10] has indicated a 20 per cent salvage of patients undergoing exenterations, and TeLinde has found anterior and posterior exenterations to have a definite place in the over-all management of these problems, although he has used the total exenteration less and less with time.

Anterior Exenteration

The anterior exenteration is a formidable procedure and one that should be undertaken only by surgeons experienced not only with the technical aspects of the operation but also with the difficult problems associated with urinary diversion. At the present time the ileal conduit is the method of choice for urinary diversion. If done properly this type of diversion eliminates the problem of electrolyte imbalance associated with ureterosigmoid anastomoses. The ileal conduit also carries with it a lower incidence of pyelonephritis but is still subject to stenosis and obstruction of the ureters at the site of anastomosis with the ileal segment.[11]

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*See Test Your Word Score Page 1639.

TABLE 3
Evaluation of Results for Carcinoma of the Cervix Stages I through IV

Institution	No. Cases Treated	5-Year Survival (%)
Graz, Austria	889	49.6
Vienna	481	54.9
Copenhagen	1567	49.0
Munich	2424	58.5
Calcutta	940	22.6
Stockholm	2056	54.5
Manchester	1760	42.1
Houston	789	63.2
N. Y. Presb.	343	48.4

Posterior Exenteration

The posterior exenteration is the least formidable of these ultraradical operations. It differs from the well accepted abdominal perineal resection mainly in that a radical hysterectomy is part of the procedure.

Certainly one should not undertake the management of malignant disease unless he is capable of offering the patient all possible modalities of therapy. Similarly, one should not undertake methods of therapy he is not qualified to administer or the complications of which he is incapable of managing. On the other hand, a physician should not deprive a patient of a type of therapy which may be of benefit simply because he is not trained to do it himself. We should not condemn methods of treatment without a fair assessment of them. The complications of exenterations are significant in both frequency and seriousness; however, it must be emphasized that these procedures are being used, for the most part, when all else has failed.

Radical Vulvectomy

Malignant lesions of the vulva constitute approximately 5 per cent of malignant lesions of the female pelvic organs. The vast majority of these cases are squamous-cell carcinoma. The treatment of this disease at present is primarily surgical and takes the form of radical vulvectomy with regional node dissection. Radiologists are not at all enthusiastic about the use of radiation therapy in the treatment of vulvar carcinoma, and its use is limited almost entirely to palliation for either far advanced cases or recurrent cases after surgery. The survival rates in Stage I carcinoma of the vulva (Table 4) are in the general range of 80 per cent. This survival rate drops precipitously in the case of Stage II carcinoma of the vulva where regional node metastases have occurred. The further decline of survival rates is seen in Stage III carcinoma of the vulva with direct extension to the anus, urethra or vagina. If these survival rates are to be

TABLE 4
Survival in Cases of Vulvar Carcinoma by Stages

	Stage I* % 5-Year Survival	Stage II % Survival	Stage III % Survival
Taussig (1917-1935)	63.6	52.6	
Way (1949-1954)	77	42	
Green (1927-1950)	86	47	9.7

*Staging explained in the text

Continued

improved, I believe more information will have to be obtained concerning lymphatic spread beyond the pelvis in those cases with positive regional nodes. Furthermore, those patients with direct extension to the urethra, anus and vagina will require more radical surgical procedures to eliminate the disease locally. The natural tendency in such cases where the urethra is involved, for example, is to transect the urethra just proximal to the gross disease in order to preserve the bladder function. The results from Green's Report as shown in Table 4 clearly demonstrate the seriousness of involvement of these structures and warrant a trial of more radical procedures rather than less radical ones.

Conclusions

Radical pelvic surgery has secured a place in the management of early carcinoma of the cervix and in recurrent carcinoma of the cervix. It is also the basic method of treatment of carcinoma of the vulva.

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The Penalty of Overweight

Imprisoned in every fat man is a thin one wildy signalling to be let out.
— Minnesota Humanist

Danger Sign

You're getting old when the narrow waist and the broad mind begin to change places. — Corn Belt Livestock Feeder

The sum which two married people owe to one another defies calculation. It is an infinite debt, which can only be discharged through all eternity.
— Goethe Elective Affinities Book 1

Neuro-Pediatrics Conference

School Failure*

Normal Intelligence — Neurologic Disease

This 8½-year-old white female was referred by Dr. C. F. Reichelderfer of Staples, Minnesota, to the University for evaluation of learning disability. Information received from Miss Charlotte Kummert, Principal of Staples Elementary School, Northside, indicated that the child has had difficulty following instructions and remembering what she has recently learned. In addition, she has great difficulty in reproducing numbers, figures and symbols.

Dr. Marcia Hyvarinen:**

This child's delivery was uneventful following an apparently normal pregnancy. Birth weight was five pounds, six ounces. Growth and development were unremarkable (aside from difficulties with her left thumb) up to the time of school participation. Because of problems in learning, she has repeated the first grade twice and now is failing a third time. Revised Stanford-Binet, administered by Dr. Ruth Hill in Staples, yielded an I.Q. of 109 on May 25, 1964. It was Dr. Hill's conclusion at that time that although the child was of high average intelligence, she demonstrated marked deficiencies consistent with cerebral dysfunction. On the basis of Dr. Hill's conclusions, special instructions were arranged in the Staples School System, which included several hours per day of home-bound instruction and one-half day in regular first grade class. The response to date from this approach has been minimal.

No clear definition was obtained as to the duration of motor difficulties noted with the left thumb. Information obtained from the mother by several different investigators suggests that the weakness may have been present since early infancy; to others the mother related that it has been

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*Held on Wednesday, March 17, 1965 at 1 p.m.

Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatric conferences are held weekly from 1 to 2 p.m. every Wednesday. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Edward C. Defoe and Dr. Charles Branthaver in Pediatrics and Dr. Robert Soll, in Adult Neurology.

**Senior Medical Student, University of Minnesota Hospitals.

Continued

present for only the last three years. The child was pulled from a couch at the age of six weeks by her older sibling; however, there is no recollection of any specific injury at that time. Whooping cough, chicken pox at eight to ten months, mumps at four years, and measles at five years were said to be mild and without after-effects. Family history revealed that the father died following an accident approximately eight and one-half months prior to the child's delivery. One older male sibling also repeated the first grade but is reported to be doing A and B work currently in school. The mother is apparently well.

The physical examination revealed a small, pleasant, dark-eyed, shy and cooperative girl. Weight and height were about the 16th percentile. Aside from neurological findings and the problems of writing and symbol recognition, nothing remarkable was found. Electroencephalograms and skull, cervical and thoracic spine X rays were within normal limits. Bone age as interpreted from wrist films was one and one-half standard deviations below the mean for chronological age.

Electromyogram showed evidence of chronic denervation in the left thenar muscles. There was also denervation in the left first dorsal interosseus, which is innervated by the ulnar nerve. The evidence for chronic denervation in the left thenar muscles was interpreted as indicative of carpal tunnel syndrome, etiology unknown. There was no explanation given as to why the ulnar innervated muscles were also affected.

Dr. Mark Nesbit:* The possibility of metabolic defect with amino aciduria was thoroughly explored in this child. However, all the tests were negative.

Dr. Paul Moe:** The history here was interesting but confusing. The birth weight of five pounds, six ounces in a child said to be full-term and possibly overdue, may be indicative of an intra-uterine problem with secondary contribution to cerebral dysfunction. Other possibly pertinent points in the history are: (1) regurgitation noted in early infancy; (2) pertussis at near the end of the first year; (3) the mother's observation that the child has always been right-handed. Regurgitation may have been a reflection of intracranial pathology. Although the pertussis was described as mild, the disease occurring in infancy must always be suspect as a contributor to pathology in a child manifesting central nervous system disease

Dominant Handedness as an Infant

Confusing was the discrepancy in the story concerning left-hand disability. As dominant handedness is not present in a child under one year, the observation of right-handedness from infancy suggests an early problem with the left arm. If this was present at birth, or following trauma at a later date, with brachial plexis stretch, it appears likely it would have been recognized and clearly related to at the time.

On physical examination, I found her left hand to be smaller than the right with the forearm 1 cm. less in circumference than the right. Tendon reflexes in the left arm were less than on the right, and left-hand strength was significantly decreased. Difficulties in grip and palmer adduction of the thumb were consistent with ulnar nerve disability. Mild dorsiflexion weakness of the wrist and opponens paresis were consistent with radial and median nerve involvement. Triceps weakness suggested C7-8 involvement. Slight pronation posturing of the left hand was also apparent. Tests for parietal lobe function, such as evaluation of textures, recognition of finger writing, et al., were not performed as well on the left as on the right. Touch and pain sensation were normal bilaterally. Cognitive* tests, such as knowledge of age, time, day, month, and year were also performed less well than one would expect for a child of this age. These observations, plus the small hand size, are consistent with a right parietal lobe lesion. Parietal lobe disease presenting prior to two years of age may produce a decrease in extremity size; after that time this is not likely to be true. However, in addition, fasciculations of the left thenar eminence and palm were noted. These are pathognomonic of a lower motor neuron lesion. So we must consider two lesions here: one in the right parietal lobe and the other most likely in the spinal roots of C7-8. As the electroencephalogram is positive in 80% in some series of children with parietal lobe involvement and reading problems, a negative electroencephalogram here is a bit unusual. The electromyogram interpretation of slowing of median nerve conduction of the wrist as being indicative of carpal tunnel syndrome is based upon very limited muscle evaluation and should be repeated. The results noted here could just as well be derived from a lesion high in the brachial plexis or cord at C7-8.

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*Pediatrician, University of Minnesota Hospitals.

**Pediatric Neurologist, University of Minnesota Hospitals.

Dr. Edward Defoe:** Is this problem with the left arm one you might expect as the end result of a Klumpke† type brachial plexis stretch?

Dr. Moe: Yes. However, that seems unlikely as there is no history of such a traumatic episode.

Dr. Defoe: What are your recommendations?

Dr. Moe: I would suggest a repeat electromyogram for more thorough muscle evaluation, and a myelogram to rule out the possibility of a neoplastic process in the area of C7-8. Myelography is a relatively benign procedure. The chances of arachnoiditis developing as a complication are minimal, if the dye is carefully removed. As to the alternatives, we can watch and see if the condition is a stable one. If we could determine that the arm problem had been present since infancy, this alternative would most certainly be the proper one.

Dr. Frank Lassman:‡

This child's reading ability was evaluated, using standard testing instruments. She was found to read at approximately the second month of the first-grade level. She is presently in the first grade for the third time. Arithmetic was evaluated similarly, and her ability to handle problems presented visually was even less than the reading ability described above. On the other hand, she was slightly improved when the problem was offered auditorily. The child's language aptitude was assessed in a screening fashion, provided by a vocabulary test. I was surprised to find a reduced vocabulary score of six years and four months (Nashville norms). The modified interpetation of this performance suggested a vocabulary level of no better than six years.

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*See Test Your Word Score Page 1639.

**Department of Pediatrics and Conference Moderator.

†See Dejerine-Klumpke Syndrome Page 1663.

‡Professor of Speech and Audiology, University of Minnesota Hospitals.

Continued

Visual Discrimination

The fact that this test required a visual stimulus as well as an auditory one should be kept in mind. Here the child is offered a word and is asked to choose from among the four pictures on the page. A primary visual discrimination deficit might influence her performance. Visual discrimination was measured using both formal (Frostig) and informal procedures. As long as the task did not involve her own motor performance, the youngster was able to score up to age. Visual motor performance fell rather significantly below the visual discrimination ability. The child was able to do quite well with visual motor performance until the task became very complex. The ability to copy directly was slightly better than copying from memory. Memory did not appear, however, to be the primary factor, but rather to introduce an additional step. The copying of the diamond figure as described in Dr. Hill's report was failed. Visual memory test was passed as long as this area was uncontaminated by the diamond-copying problem. She was entirely unable to identify letters with any precision. She failed approximately two thirds of the task requiring that she identify capital letters and small letters out of context. With regard to phonics, she was unable to associate the sound of the letter with the appropriate printed letter, or to make the sound when the letter was pointed to.

Tactile Agnosia

She demonstrated tactile agnosia.* Errors were observed when the left hand was compared with the right. On the basis of evidence elsewhere, it would be difficult to assume that this was secondary to central factors, since some peripheral damage is apparently present. She was unable to recite the alphabet, the days of the week, or the months of the year. This finding should be considered in association with the reduced vocabulary score above.

My impression was that this youngster, apparently of normal intelligence, has reduced ability in learning to read, spell and do simple arithmetic. She has a severe deficit in letter identification, tactile agnosia, and reduced verbal ability represented by reduced vocabulary and alphabet series. I would recommend that remedial reading should be continued with work at a primitive elemental level. In addition, vocabulary building should be instituted.

Dr. Moe: Does she fit the category for specific reading difficulty (dyslexia) ?

Dr. Lassman: Yes. However, this is a very broadly defined entity.

Mrs. Mary Cordingley:** The mother was interviewed to gain a picture of the present home situation and to learn about relationships with family members. The mother is a quiet woman, unable to talk freely about her situation. She reveals great tension through tremor and chain smoking. She quit school at the ninth-grade level, married at 17 and had three unhappy married years, as her husband traveled from relative to relative looking for a job. She has been widowed now for eight and one-half years and receives financial benefits from social security and several other sources. Although the amount is adequate for ordinary maintenance, she is unable to manage financially and is deeply in debt. She also has been unsuccessful in her attempts at work to supplement the income. She spends her days "bumming around" town and her evenings with her closest friends who own and work at a bar. She said she didn't mind her life; but with questioning she told of making two attempts at obtaining further education. On one occasion she spent $200 for a correspondence course and also tried an illustrator's course; but she has been unable to complete either one. She has little contact with her children; consequently they have had little opportunity for adult identification. She has, however, done a little art work with them. She feels the in-laws prefer the boy and ignore the patient. No doubt the financial situation has influenced her life. The family income will diminish in two years and end in ten to eleven years.

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*See Test Your Word Score Page 1639.

**Social Worker, University of Minnesota Hospitals.

There is great need for realistic planning for this disturbed, somewhat withdrawn woman. Supervision of the financial area should be considered. Association with an appropriate mental-health center might be arranged through the Todd County Welfare Department. The in-laws should also be considered in the planning.

Dr. Harold Ireton:* The patient was tested at the chonological age of eight years, seven months. Intelligence testing (Wechsler Intelligence Scale for Children) indicated dull-normal verbal ability (I.Q. 86) and average performance ability (I.Q. 99). Among the verbal tests most adequately performed were tests of practical judgment and abstract ability. She did relatively poorly on sub-tests measuring fund of information or arithmetic ability and vocabulary. She demonstrated average ability on all performance tests except the picture arrangement sub-test, wherein pictures must be arranged in logical sequence to tell a story. In this test, on one occasion, she arranged the story from right to left, which may be analogous to her reading reversal. Her Goodenough production was significantly below average for her age (M.A., 6.6-I.Q., 78). On the Bender-Visual Motor Gestalt she showed as striking an inability to reproduce acute angles as in attempting to copy diamond-shaped figures. Such inability at her age is strongly suggestive of some organic defect. On the basis of these results I agree that her school difficulties are not based on general intellectual deficit but rather on some more specific learning disability which is probably associated in large part with organic involvement.

The mother herself presented as a rather vague person who is little concerned about her appearance. Brief intelligence testing indicated average ability (I.Q., 105). Her Minnesota Multiphasic Personality Inventory profile, which is apparently valid, suggested considerable psychological disturbance, probably of major proportions. She acknowledges symptoms of depression, anxiety, paranoid thinking, personality disorganization and social isolation. It may be that she maintains a chronic marginal adjustment in a relatively nondemanding environment.

Dr. Defoe: Would you care to comment upon the relative effect of primary cerebral disability versus environmental factors in the initiation and perpetuation of this child's learning disability?

Dr. Ireton: Yes, both appear to be important. How to quantitate the relative importance of each is always a problem for which we have only poor answers.

Dr. Defoe: I note that the child spends one-half day in special tutorial sessions with a home-bound instructor. In view of her limited exposure to

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*Clinical Psychologist, University of Minnesota Hospitals.

Continued

contemporaries, would this not better be performed in an environment with other children where she would receive greater opportunity for socialization?

Dr. Ireton: Yes, this is important. She should have as many reassuring social experiences as possible.

Dr. Charles Branthaver:* What is the interplay between parent and child here? To be maximally effective, remedial reading activity usually needs support from home.

Dr. Ireton: The mother is somewhat empathic regarding this problem; however, I doubt if there is much meaningful support given.

Dr. Nesbit: Perhaps the grandparents should be brought more actively into a supportive role.

Dr. Defoe:

There are three major problem areas here:

Accurate Determination of the Difficulty

A repeat electromyogram should help us to more accurately determine the extent of muscle involvement. A myelogram should be done to rule out a progressive cervical cord lesion, unless with further investigation within the community, family and other appropriate sources, we can determine that this problem has been present since infancy. Without this, the possibility of a neoplastic process in the area of C7-8 cannot be logically ruled out.

Learning Problems

Remedial reading should be continued with work at a primitive elemental level. In addition, vocabulary building should be instituted (with continuing auditory reinforcement). However, as social factors may be decisive in the success or failure of such a program, environmental modification is indicated. Maximum socialization with her contemporaries within the school environment is essential. Means of moving her along in school with her social peers without increasing learning frustration should be explored. In addition, efforts should be expended to assess the home environment and the manner in which this can be made maximally supportive with a minimum of frustrations. This assessment perhaps can be arranged through the Todd County Welfare Department.

Help for the Mother

The Todd County Welfare Board should be contacted with regard to arrangements for follow-up and evaluation care at a local mental health center. In addition, perhaps some vocational training aid can be given for development of greater economic self-sufficiency.

It seems wise that responsibility for continued medical evaluation rest at the University of Minnesota until the problem with the left arm has been more clearly defined. Staples School personnel and the Todd County Welfare Department will be directly contacted by Dr. Hyvarinen and Dr. Defoe. Interpretation of the conference to the mother will rest in their hands also, with Dr. Ireton's assistance. Following this definition, responsibility for ongoing medical care and coordination with school and welfare department should reside with Dr. Reichelderfer in Staples.

Edward C. Defoe, M.D.
University of Minnesota Hospitals

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*Pediatrician, University of Minnesota Hospitals.

Acknowledgments

The moderator wishes to acknowledge the help received from Dr. Reichelderfer, the referring physician; Mr. Richard Hegre, Director of Elementary Education for the Staples School System; Miss Charlotte Kummert, Principal, and Mrs. Baker, Teacher, Staples Elementary Northside School; Dr. Ruth K. Hill, Psychologist, Staples School System; Mrs. Julia Zehnle, Caseworker, Todd County Welfare Department, in transmitting the necessary preliminary information for this conference. Unfortunately their active presence at the conference was barriered by the blizzard of March 17, 1965.

Drs. Werner Lund, J. E. Nord and P. J. Parker of Staples were also helpful in supplying data from their files.

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DEJERINE-KLUMPKE SYNDROME

This syndrome consists of paralysis and atrophy of the small muscles of the hand and forearm with an associated Horner's oculopupillary manifestation. It is the result of involvement of the lower roots of the brachial plexus and affects particularly the nerves derived from the 8th cervical and 1st thoracic roots. The interossei, thenar, hypothenar, flexor carpi ulnaris and flexor digitorum muscles are involved, associated with a lack of sensation or, on some occasions, excessive sensibility on the inner side of the forearm. Pain may be a prominent manifestation. If the sympathetic rami are involved the Horner's syndrome is present with myosis, narrowing of the palpebral fissure and recession of the eyeball.

Birth trauma with hemorrhage as a localizing lesion may be an etiologic factor or there may be a fracture or dislocation of the shoulder. Correction of the causative factor may improve the prognosis.

Durham, Robert H. — Encyclopedia of Medical Syndromes,
Hoeber Medical Division, Harper and Row, New York

No physicking. We are a machine made to live; we are organized for that purpose, and such is our nature; do not counteract the living principle — let it alone — leave it the liberty of self defence — it will do better than your drugs. Our body is a watch intended to go for a long time. The watchmaker cannot open it, and must work at random. For once that he relieves or assists it by his crooked instruments, he injures it ten times, and at last destroys it.

— Napoleon Bonaparte to his physician, Dr. Antommarchi, 1820.

The essence of style, as I see it, is the avoidance of (1) wind, (2) obscurity.

— Walter Bett, M.D., Address to the American Medical Writer's Association

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in painful shoulder

Geigy

Therapeutic Effects
The acute phase of subdeltoid bursitis, tendinitis and associated periarticular inflammation usually responds promptly and dramatically to phenylbutazone. Pain and tenderness may be relieved within 24-48 hours and mobility of the affected arm quickly restored. Full recovery is frequently achieved within 7-10 days so that therapy is generally of short duration. Calcific deposits are not specifically affected by treatment, but their presence does not appear to retard symptomatic improvement.

Phenylbutazone has not replaced physiotherapy, x-ray treatment, or local injections of hydrocortisone in the more chronic conditions, but it may advantageously be combined with these measures.

Contraindications
Edema, danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. Because of the increased possibility of toxic reactions, the drug should not be given when the patient is senile, or when other potent chemotherapeutic agents are given concurrently. Large doses of Butazolidin alka are contraindicated in patients with glaucoma.

Precautions
Before prescribing, the physician should obtain a detailed history and perform a complete physical and laboratory examination, including a blood count. The patient should be kept under close supervision and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools. Regular blood counts should be made. The drug should be used with greater care in the elderly.

Warning
If coumarin-type anticoagulants are given simultaneously, the physician should watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea and sulfonamide-type agents and insulin. Patients receiving such concomitant therapy should be carefully observed for this effect.

Adverse Reactions
The most common adverse reactions are nausea, edema and drug rash. The drug may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, generalized allergic reaction, stomatitis, salivary gland enlargement, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia are also possible side effects. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently.

Average Dosage
Initially, give 400 mg. daily (one capsule q.i.d), reducing this, if possible, when a favorable therapeutic effect has been obtained. If after one week there has been no response, discontinue the drug. Butazolidin alka contains antacids and an antispasmodic to minimize gastric upset.

Note: The physician should be fully aware of dosage, precautions, adverse reactions, and contraindications as contained in the complete prescribing information.

Also available:
Butazolidin®
brand of phenylbutazone
Tablets of 100 mg.

Geigy Pharmaceuticals
Division of Geigy Chemical Corporation
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Athletic Injuries

Injuries of the Shoulder in Athletics*

Shoulder injuries occur rather frequently in contact sports, but rehabilitation is usually not so prolonged as it is in trauma to the weight-bearing joints. Essentially, there are four injuries involving the shoulder region which concern the team physician because of their frequency of occurrence. These include sternoclavicular separation, anterior dislocation of the head of the humerus, separation or dislocation of the acromioclavicular joint, and fracture of the clavicle. Three of these problems involve only soft tissue structures; if treated properly, the athlete usually may be expected to return to competition within three to six weeks from the date of occurrence. The fourth of these, the fractured clavicle, can, in most instances, be treated by closed method, with firm union expected in eight to ten weeks post fracture.

Diagnosis

Adequate initial evaluation of a shoulder injury requires that the athlete be undressed to the waist and that the examining physician keep in mind the possible diagnoses. Momentary subluxation or dislocation with spontaneous reduction before medical examination does not mean that the treatment should be any less energetic. Visual examination for asymmetri-

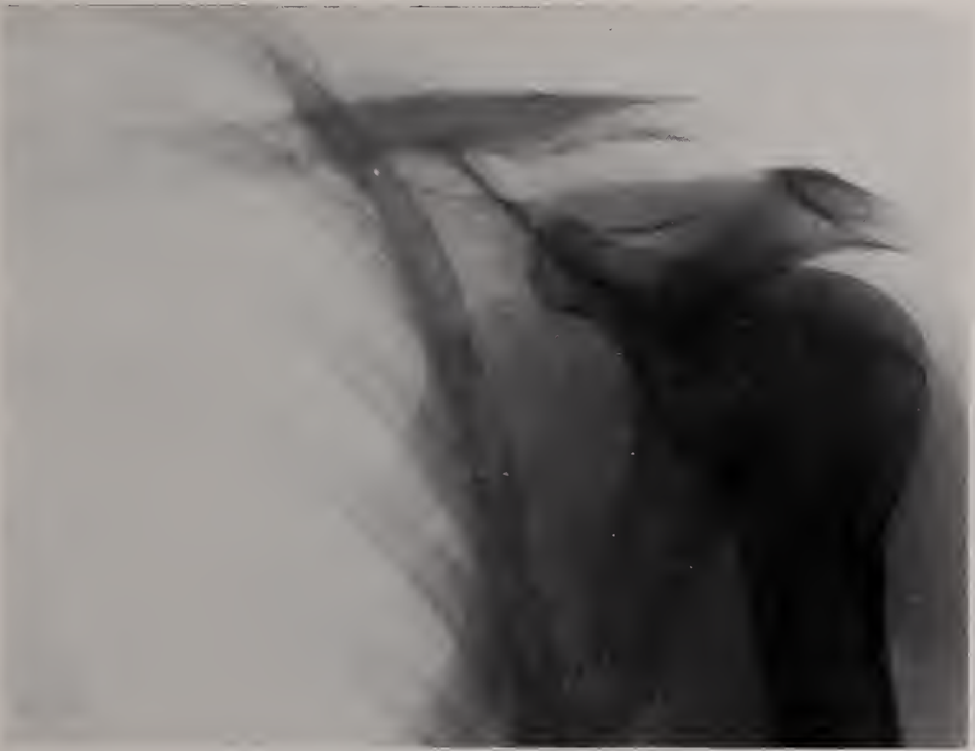

Fig. 1 — Separation of acromioclavicular joint.

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*See Minnesota Med 48:1505 for third in this series. Sponsored by Minnesota Committee on Trauma of the American College of Surgeons.

cal contours is the first step. Evidence of ecchymosis, abrasion, or hematoma helps one to focus on the specific site of damage.

Palpation adds to our knowledge of the situation; tenderness and/or crepitus are, of course, significant findings to be sought. X-rays in at least two projections are mandatory.

Treatment

If one is quite sure that there has been a subluxation or dislocation of either the sternoclavicular joint or the glenohumeral joint with spontaneous reduction, treatment in a sling and swath for three weeks is indicated. If the injury to either of these two joints requires manipulation to accomplish reduction, then three weeks of continuous sling and swath are necessary if we hope to avoid recurrent, chronic subluxation and/or dislocation. A normal sternoclavicular or glenohumeral joint can be anticipated if this rather simple treatment is insisted upon. If the reduction by the physician is necessary, it is usually best to give heavy sedation and analgesia or general anesthesia for relaxation so as to avoid further injury to soft tissue structures and hyaline cartilage. Straight traction on the arm usually accomplishes reduction of either of these two injuries if relaxation is complete. Post-reduction X-rays should be taken to prove one's clinical impression of reduction.

Treatment of acromioclavicular joint injury is more difficult and there is less agreement on how these injuries should be handled. Acromioclavicular *separation* (Figure 1) occurs when only the acromioclavicular ligament has been ruptured. Frank *dislocation* (Figure 2) occurs when the cora-

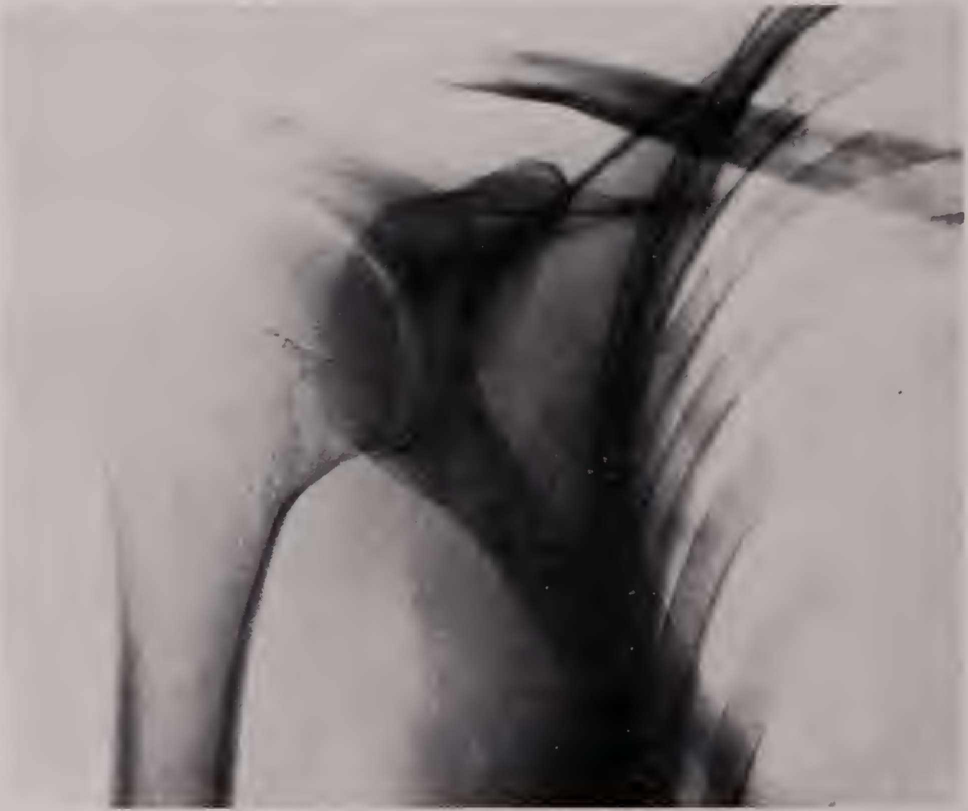

Fig. 2 — Complete dislocation of acromioclavicular joint.

coclavicular ligament, as well as the acromioclavicular ligament, has been torn. Some surgeons believe open reduction and internal fixation is warranted in both separation and dislocation in an athelete. Others feel that with mere separation, the individual is generally asymptomatic within 10 to 14 days, and that for those few who do have persistent complaints, late resection of the outer inch of the clavicle gives satisfactory function and strength. Most agree that complete dislocation in an athlete demands open reduction and some type of internal fixation for six weeks. Late onset of osteoarthritic changes at the acromioclavicular joint in those that are opened is high,[1] but resection of the outer inch of the clavicle can always be done for that eventuality. Patients with unrepaired acromioclavicular dislocations not only have a rather ugly deformity, but also often lose strength in the shoulder, especially when working with the arm above the horizontal.

Fracture of the clavicle can be treated by manipulation and application of a plaster figure-eight yoke to hold the shoulders in military position. Figure-eight straps or webbing are generally unsatisfactory, because of slipping and stretching of the straps, resulting in loss of position of the apparatus and alignment of the fracture. Caution must be exercised that the edge of the plaster does not cause pressure on the neurovascular structures in the axilla. Local instillation of two per cent procaine into the fracture hematoma affords rapid, simple, and safe analgesia for the manipulation and cast application.

Frederick E. Drill, M.D.
Minneapolis, Minnesota

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Petrus Hispanus

In his Commentaries Petrus Hispanus (c. 1215-1277), self-styled "professor of the art of medicine and investigator of the truth," revealed his empirical bent by posing such provocative questions as:

Can natural death be retarded?

How can animals who eat poisons be food for men?

Why is man less hairy and of weaker constitution than the brutes?

Why are animals soft in infancy and fruits hard?

Should paralytics eat fried fish?

Why is oil best at the top, honey at the bottom, wine in the middle of the cask?

What part of water is more truly water: top, bottom, or middle?

Why are pigs' intestines the best of animals that walk and geese's intestines of those that fly?

Is human milk subtler than asses' milk?

If the spleen causes laughter by purifying the blood, why isn't love caused by the gall-bladder?

Is raw cheese better than cooked, and solid cheese or cheese with holes in it?

Why are fools so fond of cheese?

Why does human urine enrich vines?

Are apples good in fevers?

Why pepper is good for dimmed eyes?

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Precautions: Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of preexisting symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Usual adult dosage: One or two 400 mg. tablets three times daily. Doses above 2400 mg. daily are not recommended.

Supplied: In two strengths: 400 mg. scored tablets and 200 mg. coated tablets.

Before prescribing, consult package circular.

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Child Psychiatry

Program of the Minnesota Residential Treatment Center

The Minnesota Residential Treatment Center serves emotionally disturbed children in need of intensive psychiatric treatment in a residential setting. The Center, established by act of Legislature in 1957, is administratively in the Department of Welfare. It is located at Lino Lakes, north of the Twin Cities on 160 acres of land contiguous to the Minnesota Reception-Diagnostic Center, a receiving center for children who are placed under the direction of the Department of Corrections. Both institutions are separately directed. Administrative services for both institutions, such as budgeting, inventories, payroll, personnel records, housekeeping, maintenance, and stenographic pool, are the responsibility of an administrator whose staff constitutes a unit of the Department of Administration. The first patients at the Treatment Center were admitted in June 1963. Its total bed capacity is 64 beds.

Intensive in-patient treatment is one part of a continuum of facilities for children throughout the State coordinated by the Director of Children's Mental Health Services for the State. His office integrates the medical services the State can offer to children, particularly services of institutional care and treatment. From his office come the referrals the director of the Treatment Center considers for admission. The chief criterion for referral is the likelihood that a child could benefit from intensive in-patient psychiatric treatment. Other functions of the Treatment Center are likewise related to the needs of the State.

The organization of the staff is designed to serve the multiple functions of the center and to treat a group of children which includes both sexes and a wide range of age, intelligence, and diagnoses. The age range is from six to eighteen; the I.Q.s of the patients may vary from borderline defective to superior categories; the diagnoses of the patients include severe neurotic behavior disorders, schizophrenia, autistic and symbiotic psychoses, character disorders, and chronic brain syndromes.

While a wide range of psychiatric illnesses being treated in one institution makes a need for heavy staffing, this same lack of specialization makes such an institution ideal for training students in all the disciplines involved in child care and treatment. A full and experienced staff adequately treating a wide range of problems is one essential of a good training program for psychiatrists, social workers, psychologists, students in special education, and child care workers. Providing such training is one of the functions of the Minnesota Residential Treatment Center.

Another of the multiple functions of the Treatment Center is consultation. Direct consultation is provided to the Department of Corrections for a variety of problems, from those termed "psychiatric emergencies," to aid

Continued

in long-term planning for particular children in custody. Direct consultation on matters of programming for child care is available to other institutions — those newly developing child treatment programs, for instance. For difficult diagnostic problems, especially those needing a period of study with the patient in residence, diagnostic services of the Treatment Center are available to agencies throughout the state.

Organization of staff and staff activities is based on the following assumptions about treatment: (1) a rational plan of psychiatric treatment requires thorough diagnostic study and skill in diagnostic formulation; (2) individual psychotherapy is one element of intensive treatment which takes fullest advantage of therapeutic possibilities in the shortest possible time; (3) greatest effectiveness in an intensive treatment program is attained when all the child's daily activities and contacts are attuned to the specific aims of a treatment plan arising out of the diagnostic formulation. Implicit in these assumptions is the view that residential treatment, even when lengthy, is an interlude in the patient's life, not a way of life.

The plan of psychiatric treatment for each child is the psychiatrist's responsibility. In addition to the medical director, who has over-all responsibility for all aspects of the program, two staff psychiatrist positions are allocated for the Treatment Center. (To date these two positions have not yet been filled so that the program is accordingly adjusted temporarily to the limits of what psychiatric staff work the medical director can do.) The work of the staff psychiatrists includes: (1) presiding at staffings; (2) direct psychotherapy; (3) supervision of psychotherapy; (4) psychiatric consultation to other staff members and to other institutions, particularly to the Minnesota Reception-Diagnostic Center, our next door neighbor in the Department of Corrections; and (5) teaching.

The psychology staff consists of a chief psychologist and two staff psychologists. Their responsibilities include: (1) diagnostic testing of children who are being considered for admission and of those who are about to have review staffing of their cases; (2) direct psychotherapy; (3) teaching; and (4) consultation to other staff members, especially on research and related matters.

The departments of child care and social service are under one department head. This permits better coordination of such things as planning visits from relatives with the scheduling of child care activities for the child, so that one doesn't become disruptive to the other. More important, it tends to keep child care from becoming an usurpation of parental responsibilities rather than a distinct discipline in an interdisciplinary treatment effort. There is a constant danger in residential treatment programs that the child's direct appeal to child care workers for help of every kind will make of the child care worker a parent substitute attempting to provide in myriad ways a new life with the promise of permanency. At the Treatment Center the person responsible for all child care is also responsible for the casework with parents. The aim of supporting parents in their parenting and in the hope of a child's return to family life is best served if parents correctly see the aim of child care in the institution as treatment and not as substitute home care.

The child care staff includes the department head already mentioned, two assistant supervisors, and forty-six child care workers. There are four cottages in the institution, two eight-patient living units to a cottage, or eight units in all. Each unit is staffed by four child care workers for three shifts. The children are grouped according to age, but on any one unit this may be the only common denominator; the range of intelligence and kinds of illness make individualization of care necessary. The living units are separated from each other geographically (except for the twin units which comprise a cottage) so that a child care worker cannot easily call on a worker in another unit for help in times of need for heavier staffing in his living unit. As a partial remedy for this, child care workers who are best qualified are designated "charge counselors." It is their duty to circulate among the cottages and provide help in many ways and to contact the assistant supervisors, the department head, or the director when they see the need.

The relevance of child care measures to the treatment plan is reviewed often in both scheduled and informal meetings with the two assistant supervisors and the department head, such meetings being the confluence of supervision and in-service training. The head of the department of child care is responsible for an in-service training program of lectures and discussions for child care workers. The lecturers are chiefly from the Treatment Center staff but there are also guest lecturers from outside the staff. Teaching and supervision are purposely fused; the department head and his two assistant supervisors work at welding usable concepts of psychiatry, psychology, and social work on the one hand to the practices of child care on the other so as to avoid the discontinuity between these which so often lies behind the woes of residential treatment centers.

The social work staff consists of the department head already mentioned and three staff social workers. They (1) interview parents or guardians to gather diagnostic information prior to a child's admission and also gather information from all other contributing sources; (2) work out with parents, or whoever is responsible for the child, what amounts to a contractual understanding, prior to admission, of what the Treatment Center can attempt as a feasible plan of treatment and what will be needed for such treatment in the way of involvement of parents in future interviews, visiting, trips home, provision for the child after he leaves the Center, etc.; (3) maintain from the beginning of the diagnostic study and throughout the treatment a liaison with whatever community resources will support a long-term plan for the child; (4) conduct scheduled interviews with the parents throughout the child's treatment at the Center, with aims and methods in keeping with the treatment plan for the child and the contractual agreement with the parents or others, utilizing in this interviewing whatever is known of the current issues in the child's life in the institution and in his psychotherapy; (5) convey to the rest of the staff the social worker's own understanding of what forces are operating within a family as this understanding develops; (6) conduct psychotherapeutic interviews with children as assigned by the director; (7) teach social work students.

Many of the children in residential treatment have not only dropped years behind in their academic education because of their emotional illnesses but have also not played sufficiently or interacted with others sufficiently in a secure environment to have developed ordinary skills or habits or graces which are usually taken for granted. Even if such children

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could be "cured" overnight of their emotional problem they would still be seriously handicapped. At the Treatment Center, activities provided by a recreation worker, a music therapist, and an occupational therapist have as their aim the correction of these developmental lacks and distortions. The establishment for the child of a sense of rhythm, a sense of his own body, the satisfaction of using his muscles in an effective and graceful way and of coordinating his eyes and hands to accomplish something — these may be a "sine qua non" of treatment for an individual child and can accelerate treatment gains for many others.

The head of the activities department is also the head of the department of special education, having a background in both disciplines. Since few patients are able to attend public school the three teachers in the latter department provide teaching for almost all the children. Their focus is on academics and the attempt to further the child's pursuit of knowledge, to satisfy his curiosity and to give him what knowledge is considered useful in our culture, which is no different from the same attempt in the public schools. The teachers at the Treatment Center do not function as therapists using educational techniques but as teachers who are sophisticated about psychological and developmental issues.

The department head in charge of child care and social work and the department head in charge of special activities and special education are jointly responsible for translating the treatment plan that comes out of a staffing into specific programming for the child. An integrated program in terms of hours in cottage activities, in special activities, and in school, is devised in keeping with the treatment plan which is stated more generally, in terms of approach, aims, attitudes, and needs for certain kinds of experience.

General medical, dental and nursing care are provided for children from the Center and from the neighboring corrections institution by a physician, dentist and nurses accountable to the medical director. Appropriate clinics and hospitals outside the Center are used also.

The entire staff is involved in a program of staff development which is open as well to personnel from other institutions. The regular weekly scheduled exercises are made to serve, as far as possible, teaching functions in addition to getting the necessary staff work done. A weekly staff development meeting allows an opportunity for each staff member to present his point of view about what he does and what others do. Closely tied to the striving for the best possible treatment for each child is a program for continuous professional growth since ultimately, no matter what the organization of any program, therapeutic experience for the patients depends on the competence and morale of the staff.

Fred Kane, M.D.
Minneapolis, Minnesota

Editors Note: Because the Minnesota Residential Treatment Center is so limited in capacity (64 beds), all requests for admissions must be made by the County Welfare Department office and submitted to the Director of the Children's Mental Health Services for review.

Let thy mind's sweetness have its operation upon thy body, thy clothes, and thy habitation. — Herbert

Clinical Path Conference

Rectal Bleeding

This 49-year-old female entered the hospital because of rectal bleeding. Intermittent episodes of bright red rectal bleeding had occurred for one year.

Similar episodes had occurred twenty years earlier but had subsided to occasional episodes of spotting, until frank, painless bleeding associated with defecation was noted. Rectal pain "like little needles" also developed during the year. Anorexia, associated with weight loss of an unknown amount, was also present, and the patient had been unable to work for the preceding three months because of increased weakness. She was known to have hemorrhoids and was generally constipated. Some narrowing of her stools had apparently been observed for some time. Mineral oil was often taken and tended to produce diarrhea. There was no history of melena, food intolerance, abdominal pain or jaundice. Anemia had been diagnosed some years earlier and the patient had taken some iron pills.

Migratory polyarthritis had been present for four or five months, 15 years prior to admission. This was treated with injections of unknown medication. Pelvic inflammatory disease had been treated twenty years earlier by operation. Her last menstrual period occurred ten years prior to admission.

Physical Findings

Examination revealed a well-developed, anxious female in no distress, who complained of rectal pain.

The mucosae and nail beds were pale. The lung fields were clear to percussion and auscultation. The heart sounds were distant. The point of maximal impulse was at the fifth left intercostal space at the midclavicular line. M1 exceeded M2, and A2 exceeded P2. No murmurs were heard.

The costovertebral angles were nontender. The abdomen was soft, nontender, and tympanitic to percussion. No organomegaly was palpated. Bowel sounds were hyperactive. A cystourethrocoel and small rectocoel were found on pelvic examination. The cervix descended to the introitus with straining.

A small amount of pink fluid was present within the extremely tender anal canal. A circumferential stricture was palpated approximately 3 cm. above the internal sphincter. No masses were palpated and no external hemorrhoids were seen.

The blood pressure was 104/70 mm. Hg.; the pulse 112 per min.; the respiratory rate 16 per min., and the temperature 100.2°F.

Laboratory Findings

The hemoglobin was 9.5 gm. per cent; the white-cell count was 14,400 per cu. mm. Urinalysis was negative. The blood urea nitrogen was 9 mgm. per cent and the glucose 115 mgm, per cent. The electrolytes were within normal limits, as were the liver function studies, save that the albumin-globulin ratio was inverted, with the albumin level being 3.7 gm. per cent and the globulin level, 4.0 gm. per cent. An electrocardiogram was

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unremarkable and a chest x-ray normal. A plain film of the abdomen showed a nonspecific pattern of gas within the small and large bowel.

Proctoscopy revealed some internal hemorrhoids and a stricture at 5 cm., beyond which the scope could not be passed. Bleeding from above this level was seen. Biopsies were taken.

A Frei test was negative. A barium enema revealed a 6-cm. area of deep, irregular, ulceration in the rectosigmoid. The descending colon appeared to be shortened and the sigmoid decreased in length. There was loss of haustral markings in the descending colon.

An intravenous pyelogram revealed a double collecting system at the right kidney but no other abnormality.

Progress

During this period the patient continued to bleed and received 1500 cc. of whole blood to raise her hemoglobin to 10 gm. per cent.

Operative Procedure

She underwent colon resection, including proctectomy, during the third week of this hospitalization. Her postoperative course was satisfactory and she was discharged from the hospital.

Readmission

She was readmitted to the hospital three months after her operation because she had become progressively weaker and had again begun to bleed from her distal intestinal stoma. She had also developed exertional dyspnea and dizzy spells.

Physical Findings

Examination at this time revealed a thin, wasted female, who was exceedingly lethargic. The lung fields were clear. Generalized abdominal tenderness was present. Hepatomegaly was noted. Bowel sounds were heard. A granulating wound was present at the perineum.

Laboratory Findings

The vital signs were similar to those of her previous admission, except that the temperature was now 101 degrees F. The hemoglobin was 7.5 gm. per cent and the white cell count 21,900 per cu. mm. The blood urea nitrogen was 7 mgm. per cent and the sodium was 138 mEq/liter, the potassium 3.3 mEq/liter and the chloride 105 mEq/liter. The CO2 was 31 mEq/liter. The thymol turbidity was 10 units, the cephalin flocculation test 1 plus and the total protein 6.8 gm. per cent, with the albumin 2.4 gm. and the globulin 4.4 gm. per cent. The prothrombin time was 15.8 seconds and the control 12.6 seconds. The calcium was 13.5 mEq/liter and the phosphorous 3.0 mEq/liter. The alkaline phosphatase was 12.9 King-Armstrong units.

A chest x-ray was normal. A plain film of the abdomen showed a moderate amount of gas within the bowel. An upper GI series was normal. A small bowel series suggested a possible fistula between the distal ileum and perineum. Five small areas in the left lobe of the liver showed no uptake of radioiodinated Rose Bengal, and the inferior border of the liver was markedly serrated.

Progress

The patient became increasingly lethargic and required tube feedings and supportive infusions of plasma.

Blood cultures and a lumbar puncture were unrevealing. Her urea nitrogen rose to 70 mgm. per cent.

She died quietly five months after her laparotomy.

Discussion

Dr. Harry Z. Mellins*

Any ulcerating lesion in the bowel can produce rectal bleeding; there aren't many lesions, however, which can cause both pain and bleeding. We can therefore narrow the field to lesions which produce stricture or a mass with ulceration. Also to be considered are lesions which may produce a mass associated with fissure formation and spasm. Similar episodes had occurred twenty years earlier but had subsided to occasional episodes of spotting, until frank, painless bleeding associated with defecation was noted at the beginning of the year. The question that arises is how similar were these episodes? This is a woman reportedly known to have had hemorrhoids, and one has to determine whether these were indeed similar episodes, or whether her earlier bleeding could have been due to her hemorrhoids. If one is to believe the history as given, then one has to think of a process that has continued for twenty years and then reached an acute terminus at this time. The history of constipation and narrowing of her stools tends to go along with the possible diagnosis of a stricture in the lesion. She had been known to be anemic, which, of course, would be associated with the bleeding. The past history I cannot find very helpful in evaluating the present illness. Except for the finding of a circumferential stricture 3 cm. above the internal sphincter, which we suspected from the history, physical examination was not especially striking. She was pale, with a very low grade fever and a slightly increased pulse, which would accompany her anemia, with perhaps some associated inflammatory process.

She had a hemoglobin of 9.5 gm. and her white count was slightly elevated. The blood urea nitrogen was within normal limits, but slight elevation of the glucose was present. Reversal of the albumin-globulin ratio was noted. At proctoscopy, which revealed some internal hemorrhoids, bleeding was seen to be coming from above the stricture. At this point we will turn to the films. Barium enema shows an area of narrowing in the rectosigmoid and sigmoid at least four inches in length. This area is irregular in outline, suggesting ulceration, and contains multiple small filling defects suggesting a polypoid lesion. The rectum itself seems small also and cannot be identified. There seems to be the edge of a tumor mass in the proximal portion of the straightened, shortened sigmoid. The evacuation film shows a normal mucosal pattern throughout the ascending and transverse colon, with a normal type of collapse. There is loss of the normal accordian-pleated collapse in the descending colon, with straightening of the descending colon. Differential diagnosis of this kind of straightening

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is usually one of two things: a normal finding not uncommonly seen in people addicted to laxatives, or a sign of ulcerative colitis limited to the descending colon. The latter, however, is a somewhat dangerous diagnosis to make, because a good many normal people have this loss of haustrations. The air-contrast study also suggests that there is some rigidity with some loss of expansibility of the entire descending colon. Because of the findings present in the colon, the possibility of ulcerative colitis of many years duration, with superimposed malignancy, would have to be very strongly considered. This does occur in women of this age group and would account for a process which gives pain, bleeding and debilitation, with a 20-year history. Such malignancies metastasize early and widely.

The next possibility would be Crohn's disease of the colon (granulomatous colitis), which can be limited to the left side, although it is most frequently seen in the ascending colon and cecum. It usually causes diarrhea, rather than constipation, and generally produces a polypoid lesion, which would account for the rigidity and the shortening of the descending colon. Another possibility is linitis plastica of the colon.

Without clinical evidence of ulcerative colitis, we would assume that the appearance of the descending colon was a normal variant. Sarcomas of the colon occur but are quite rare. One of the lesions that occasionally occurs in the colon and that can cause anemia is lymphosarcoma. Syphilis seldom gives a local stricturing like this; it tends to involve the colon widely. Lymphogranuloma can cause such narrowing of the colon but is almost always associated with sinus tracts, and there are no sinus tracts visible here. We also have a negative Frei test. Schistosomiasis can involve the rectum and cause narrowing; it does not usually involve the sigmoid, however, and there are no other findings to suggest schistosomiasis.

In reviewing the small bowel, multiple small nodular filling defects were found on two different examinations. Now these nodules (intraluminal) are present on two separate small-bowel studies. Unfortunately one has to be very wary about diagnosing defects of this kind. It is desirable to fluoroscope the patient at the time one of these is seen and to spot-film it to be sure that it is not an air bubble. Inasmuch as these nodules appear on two different examinations, although they do not match up on the two, I am forced to consider that they may represent intramural or intraluminal nodules projecting into the lumen of the small bowel. If this is correct, we then have to consider what other lesions metastasize to the small bowel and give nodular densities. There are three common ones that do: melanoma, which may produce the so-called "target cell" metastases, when submucosal or subserosal implants ulcerate; lymphosarcoma; and some carcinomas. The other x-ray studies are not remarkable. The patient was operated upon and we are told that a colon resection, including proctectomy, was done, supporting the thesis that this was a wide-spread lesion that involved the rectum as well as the adjacent descending colon and sigmoid.

The remainder of her course does not require much discussion. Except that the potassium is a trifle low, the laboratory findings are not particularly helpful. Evidence of liver disease is present, with abnormal thymol turbidity, prothrombin time, and alkaline phosphatase values. Liver involvement is also suggested by the fact that there are five small areas in the left lobe of the liver which show no uptake of radioiodinated Rose Bengal and by the fact that the inferior border of the liver appears serrated.

Multiple hepatic abscesses might produce this picture. Wide-spread metastasis, however, is also suggested by the elevated calcium. We know that in disseminated malignancy, hypercalcemia may be found. There is no evidence of multiple bone lesions on the films available.

In summary then, I believe this patient had left-sided ulcerative colitis with malignant degeneration and metastasis to the small bowel and liver. Lymphosarcoma is a second possibility.

Pathology

Dr. Stanley Minkowitz*

Proctoscopy had revealed a stricture 5 cm. from the anal verge. This was hard to believe because examination of the biopsy specimen removed from this area contained epidermoid carcinoma. Epidermoid carcinomas usually occur either at the anal verge, or somewhat proximal to it, but very rarely at 5 cm., where the biopsy was reportedly taken, or at higher levels. Total colectomy with resection of the terminal ileum and proctectomy produced a specimen that measured 130 cm. The sigmoid was slightly shortened, but the length of the entire specimen was within normal limits. In the area of the splenic flexure, there was a small, ulcerated, saucer-shaped lesion that was very firm in consistency. The descending colon was somewhat narrowed, the most severe narrowing being seen in the sigmoid colon, the lumen of which was about one third normal in width. A little dilatation was

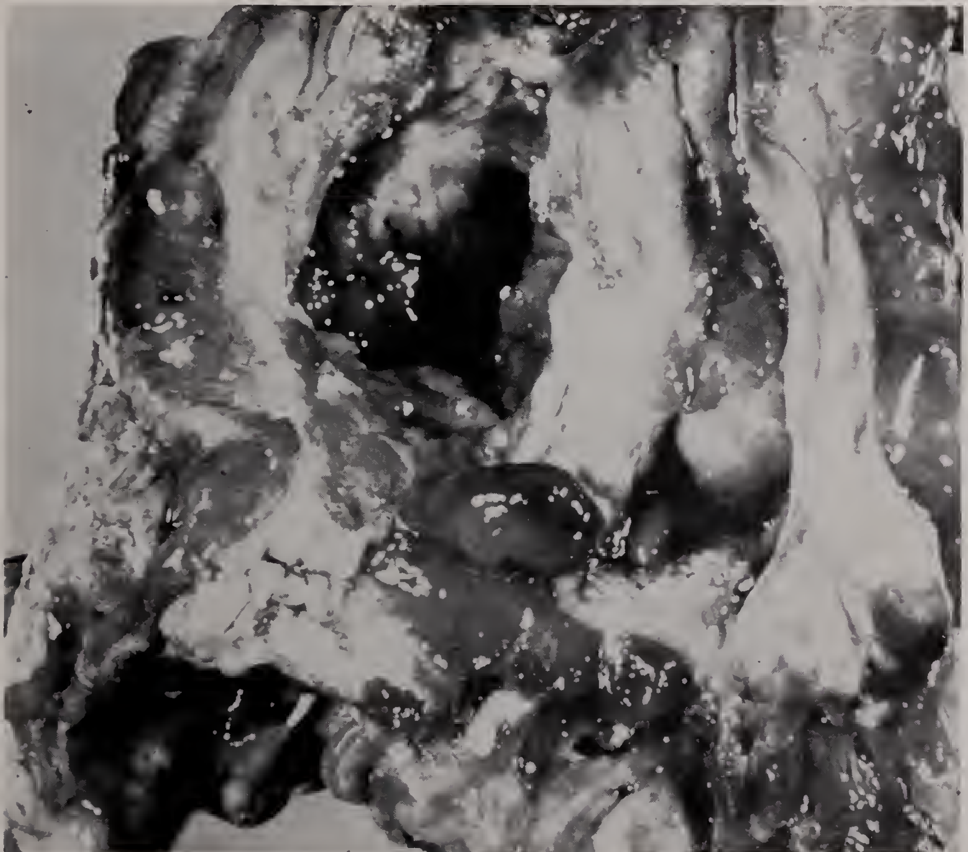

Fig. 1 — Rectosigmoid area with ulceration and squamous metaplasia.

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present in the rectal area. The mucosa of the rectum and the sigmoid was completely eroded, except where smooth, shiny, whitish linear discolorations were present. These represented leukoplakia or squamous metaplasia and were also present proximal to the lesions (Fig. 1). No pseudopolyps or "mucosal bridges" were seen and there were no signs of a chronic inflammatory process.

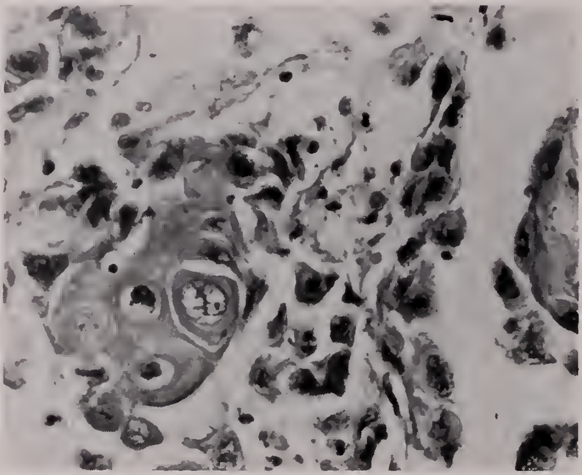

Fig. 2 — Squamous-cell carcinoma with pearl formation. Hematoxylin and eosin. X 100.

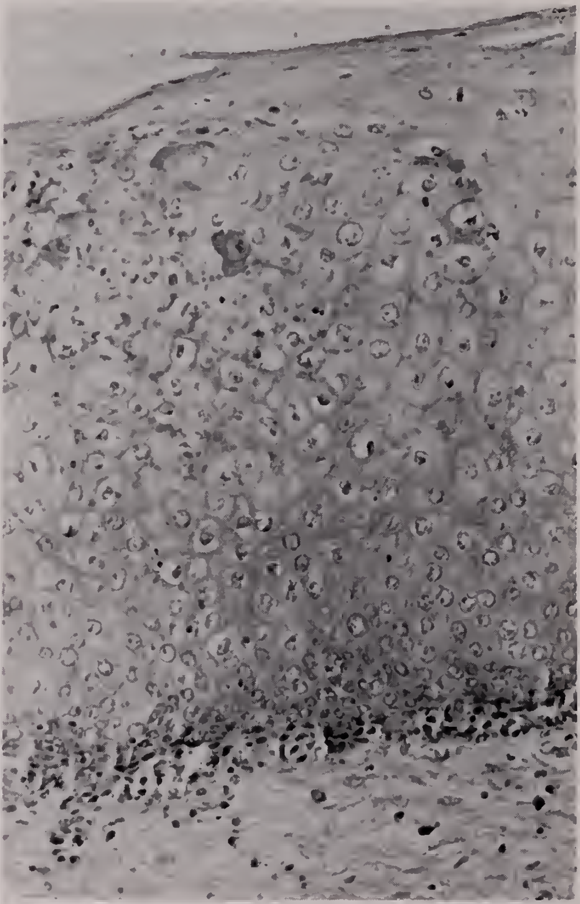

Fig. 3 — Squamous metaplasia in rectosigmoid area. Hematoxylin and eosin. X 40.

Microscopic examination of the lesion showed infiltrating malignant epidermoid cells forming pearls (Fig. 2), many of which contained large amounts of keratin and were arranged in nests. Some areas were moderately undifferentiated. Squamous elements within adenocarcinomas are not unusual; adenoacanthomas, for example, may be found in the bowel. A somewhat unusual finding in this case was the fact that there were no malignant adenomatous structures present. Associated with the squamous-cell carcinoma were areas of squamous metaplasia, in some areas of which the epithelium looked absolutely benign (Fig. 3), and in other areas of which, carcinoma in situ was present (Fig. 4). Outside the ulcerated areas, between the whitish areas containing the squamous metaplasia, normal colonic glands were present (Fig. 5). There are various theories concerning the etiology of these squamous cells. One theory is that they are ectopic rests, but this theory doesn't seem to be applicable in this case inasmuch as they are present over an extensive area. You wouldn't expect to find ectopic rests throughout the entire left side of the colon. The other theory is that they come from undifferentiated basal cells; but this theory is difficult either to prove or to refute. Another possibility in some adenoacanthomas of the bowel is that cells of adenocarcinomatous character become undifferentiated and then form squamous-type cells. In this case, however, there is no evidence of any adenocarcinoma. Probably the most likely theory is that these squamous cells represent a metaplastic phenomenon occurring within the adenomatous structures of the colon. What causes this metaplasia is unknown. It can be hypothesized that some sort of carcinogen has acted on the colonic mucosa to produce the squamous metaplasia and that further exposure to this material has caused the squamous-cell carcinoma of the rectosigmoid area. This happens to be an extremely unique case. I haven't found another in the literature exactly similar. Squamous-cell carcinomas of the right colon have been reported in two patients.[1,2]

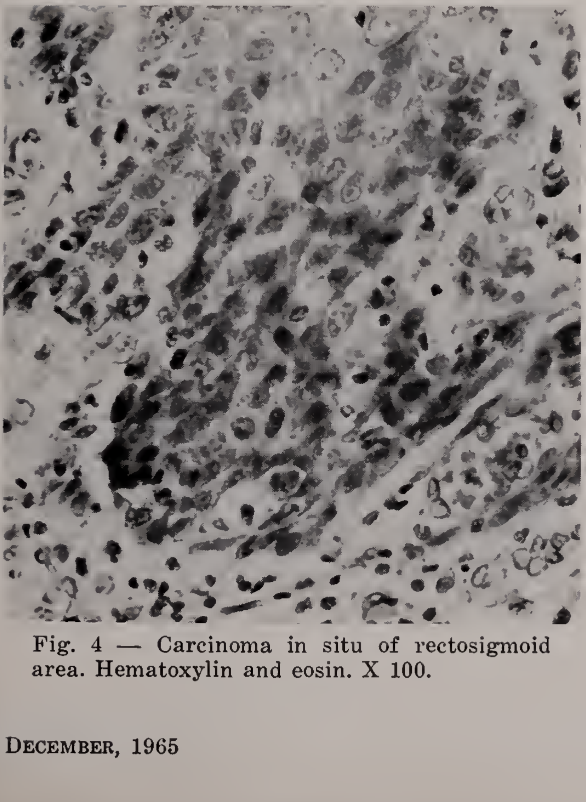
Fig. 4 — Carcinoma in situ of rectosigmoid area. Hematoxylin and eosin. X 100.

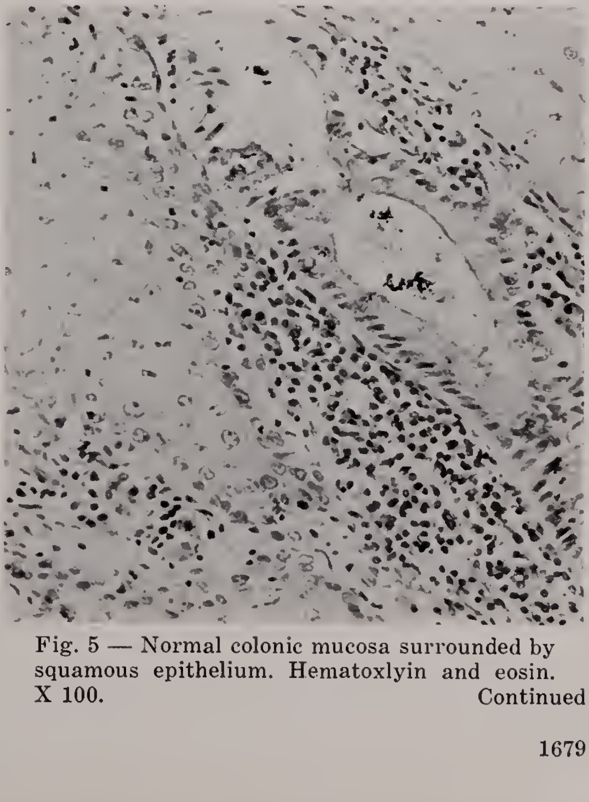
Fig. 5 — Normal colonic mucosa surrounded by squamous epithelium. Hematoxlyin and eosin. X 100.

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As no autopsy was obtained at the time of the patient's death, we don't know whether or not there was small bowel or liver involvement by this neoplasm or any other process during her terminal period.

Final Anatomic Diagnoses

Squamous-cell carcinoma of the rectosigmoid with metastasis to the splenic flexure.

Extensive squamous metaplasia of the descending colon, sigmoid and rectum, with areas of carcinoma in situ.

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"Skal noe gjøres, så få det gjort"
If something must be done, then get it done

Thus counsels an old Norwegian motto which reflects the attitude of a sensible people preconditioned by a rugged history to face facts and then take action. — THE AMERICAN SCANDINAVIAN REVIEW — Autumn 1965

Ramon Lull

In his Contemplation of God Ramon Lull (1235-1315) deplored the fact that doctors of the body are more sought after, better paid, more scrupulously obeyed than are physicians of the soul. They go well clad on good steeds, and amass wealth by working all sorts of impositions upon their patients, boasting of their knowledge of diseases of which they are really ignorant, prolonging the period of illness in order to increase their pay, and prescribing syrups and the like in large quantities because they share in the profits of the apothecaries. They try out potions on their patients which they would never take themselves, and there is no other art in the world so risky and over which there is so much disagreement.

Lynn Thorndike in A History of Magic and Experimental Science.

Medical Conference

Diagnosis of Hyperparathyroidism

Dr. Richard Rosen*

During the past several months, we have encountered a number of patients with hyperparathyroidism. This symposium will present an interesting case that will serve as an introduction to a discussion of the diagnosis and treatment of the disease.

Dr. Carl Grosz**

A 31-year-old negro female was admitted to Kings County Hospital because of nonradiating epigastric pain of one day's duration. She had had a similar episode four months before which also lasted one day and subsided spontaneously. Her alcoholic intake consisted of one pint of gin per weekend. On admission, her blood pressure was 128/94, pulse 110, respiration 22 and temperature 99°F. The hemoglobin concentration was 14 gm.% and the leucocyte count 12,400 per mm^3. The serum amylase was 550 Somogyi units. Physical examination was unremarkable except for epigastric tenderness. X-rays of the abdomen were not helpful. She was treated for acute pancreatitis with nasogastric suction, intravenous fluids, tetracycline, Probanthine and analgesics. The following morning the serum calcium and phosphorus determinations were 14.5 mg.% and 3.5 mg.% respectively.

Dr. Richard Rosen

This patient was subsequently shown to have persistent hypercalcemia; her serum calcium levels ranged between 12.5 and 16.1 mg.%. This is presumptive evidence for hyperparathyroidism and indicates a need for further evaluation. The differential diagnosis should include chronic renal disease with secondary autonomous hyperparathyroidism, milk-alkali syndrome, sarcoidosis, vitamin-D intoxication, metastatic carcinoma, and multiple myeloma. Some of these entities are more common causes of hypercalcemia than of hyperparathyroidism. A normal intravenous pyelogram, serum creatinine, blood urea nitrogen and urinalysis ruled out primary kidney disease in this patient; normal gastrointestinal x-rays and lack of medication history ruled out vitamin-D intoxication and the milk-alkali syndrome. A normal chest x-ray and a negative steroid suppression test made sarcoidosis unlikely. The steroid suppression test, which can be helpful in evaluating hypercalcemia, consists of giving 10 mg. of prednisone four times a day for seven days and determining its effect on the hypercalcemia. In this patient, a bone survey was negative except for loss of the lamina dura of the teeth and, together with a negative steroid test

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and a normal serum alkaline phosphatase, also made metastatic bone disease unlikely. The urine was negative for Bence-Jones protein, and bone-marrow examination and the serum electrophoretic pattern were normal, ruling out multiple myeloma. The factors in favor of a diagnosis of primary hyperparathyroidism included the persistently elevated serum calcium, hypercaliuria which persisted on a low calcium diet (urinary excretion of 328 mg. Ca per day on a 125 mg. Ca diet), no change in the serum calcium with steroids, loss of the lamina dura, and an abnormal tubular phosphate resorption test (TRP). Tubular phosphate resorption is perhaps not as well known as some of the other tests of parathyroid function. It can be determined from the formula.

$$\text{TRP} = \left[1 \frac{\text{Urinary P x Serum Creatinine}}{\text{Urinary Creatinine x Serum P}} \right] \text{x } 100$$

The normal is 82 to 95%, and a value under 60% is considered diagnostic of hyperparathyroidism. This patient had a value of 40%. Consequently, a neck exploration was performed.

Four parathyroids were easily identified and all were about three times normal size. Two of these glands were removed and the remaining two biopsied. Frozen sections confirmed that all four were parathyroid glands. It was thought that this was a case of primary parathyroid hyperplasia. On further exploration, another tumor was found: a large mass about 5 cm. in diameter, paratracheal and retroclavicular in location, projecting into the neck. This tumor was removed and also proved to be parathyroid tissue. The incidence of multiple parathyroid glands, that is, more than four, is well described in the anatomical literature and fairly well described in the pathologic literature; but it is seldom stressed in the surgical literature. Up to 12 parathyroid glands can be present normally; no good figures exist as to the incidence of an excessive number. Usually a surgeon, after identifying four, does not look for others. This case indi-

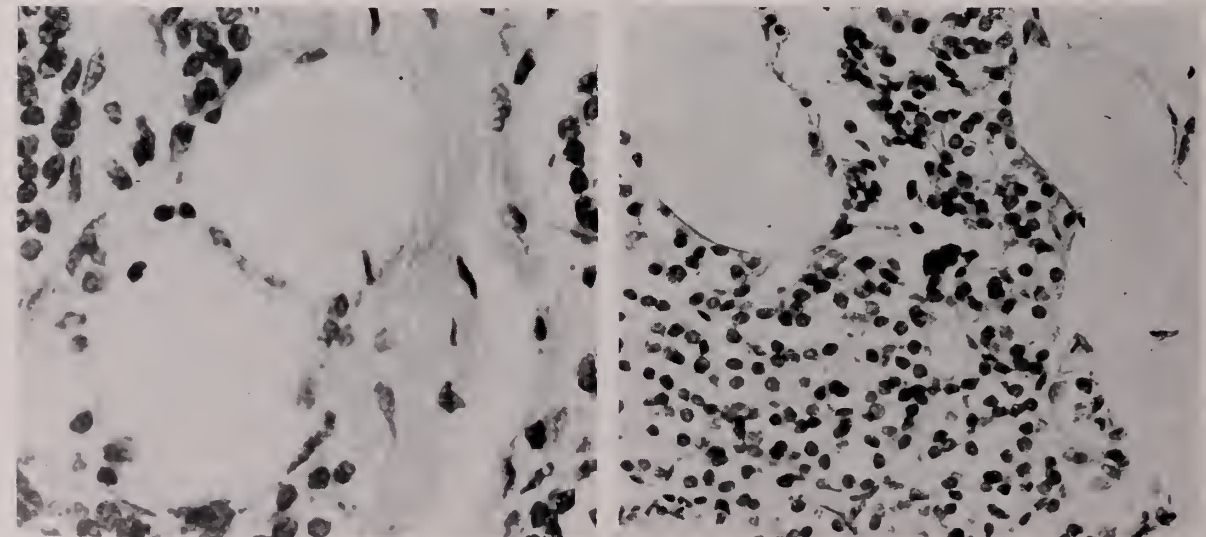

Fig. 1 (a) Biopsy of left superior parathyroid gland showing fat cells and chief cells. Hematoxylin and eosin. X 200. (b) Normal parathyroid with fat cells, clear cells and chief cells. Hematoxylin and eosin. X 200.

cates that a careful search of the neck and the available superior mediastinum should be made even when four parathyroids are identified.

Dr. Stanley Minkowitz*

The diagnosis of a normal parathyroid on biopsy is based on the finding of fat within the gland. This fat may be focal, and if an area containing fat is not included in the biopsy, the gland would look like a hyperplastic gland. A biopsy diagnosis of an adenoma is even more difficult. The diagnostic criteria require a rim of normal parathyroid around a circumscribed area of hyperplastic parathyroid and the finding of normal parathyroids elsewhere.

The case presented illustrates our problems. The right superior parathyroid was removed and was normal. The left superior gland was biopsied and reported as hyperplastic on frozen section, but the paraffin section revealed fat cells (Fig. 1a) ; however, the gland is normal, although enlarged. The left inferior gland was biopsied and was also normal (Fig. 1b). The right inferior gland was removed and was reported as hyperplastic, because no fat was seen; in addition, the large paratracheal gland that was described was removed. It measured 4 x 3 x 2 cm. and weighed 10 gm. Normally the parathyroids measure 0.5 x 0.4 x 0.2 cm. each and weigh about 35 mg. altogether. Grossly, this entity looked like an adenoma, but no rim of normal tissue could be identified, although sometimes there is so little normal tissue present that it can be difficult to find.

You can not predict the glandular function or history by the cell type. The main cell found in the parathyroid is the chief cell. This is a small cell type with a large nucleus and very little cytoplasm. The other cell types are supposed to originate from this chief cell. If it contains much

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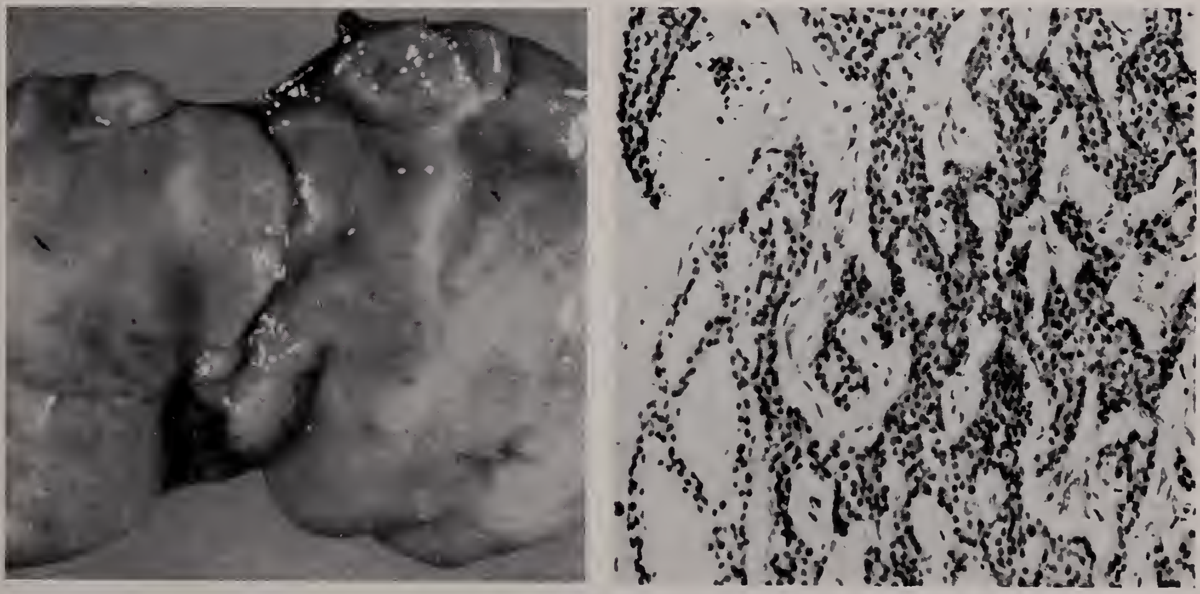

Fig. 2 (a) Cut surface of the parathyroid adenoma. Gross picture. (b) Microscopic picture of the adenoma. Hematoxylin and eosin. X 200.

clear cytoplasm it is called a clear cell or Wasserhelle cell. If the cytoplasm becomes eosinophilic it is called an oxyphil cell, which is supposed to be nonfunctioning.

In this case, then, we have two parathyroids removed that were hyperplastic, one that was normal, and two biopsied that were normal. I think that this probably represents two adenomas rather than hyperplasia.

Dr. Carl Grosz

Mixter and Cope collected 62 patients from the literature with hyperparathyroidism and pancreatitis. In their own experience, 7% of patients with hyperparathyroidism had pancreatitis or pancreatic calculi. Very few of these were alcoholics. Fifteen of the 62 patients died of pancreatitis, indicating the seriousness of this complication. The calcifications seen on abdominal roentgenograms are usually in the ductal system. McPherson has given animals large doses of parathormone and has observed calcium deposits in the omentum, but he was unable to reproduce the pancreatic ductal calcification.

Dr. Stanley Wallach*

Hyperparathyroidism is a disease which dates from antiquity, and it is often forgotten that the isolation and purification of the hormone was not accomplished until about five years ago. Since that time a great deal has been learned. Parathormone is a polypeptide with a molecular weight of about 9,000 and has a multiplicity of actions. The main purpose of this hormone is to maintain serum and extracellular calcium concentrations at levels which will provide sufficient calcium to the cell for normal neuromuscular and cardiovascular function, endocrine and exocrine secretion, mitochondrial function and other physiologic and biochemical processes.

The hormone has at least three recognized actions on calcium metabolism. It causes the resorption of previously formed bone by converting osteocytes and osteoblasts to osteoclasts which presumably produce metabolic acids capable of dissolving bone. The calcium so released provides a supply for the maintainence of the plasma calcium level. The hormone also increases gastrointestinal absorption and renal tubular reabsorption of calcium. The phosphaturic action of the hormone, which is effected by decreasing phosphorus reabsorption by the renal tubules, can be considered ancillary to the hormonal action on calcium metabolism. When bone is resorbed, both calcium and phosphorus are released; if the latter accumulated in the extracellular fluid, calcium phosphate complexes would be formed which would be readily shunted to soft tissues and bone. Therefore, the hormone's ability to maintain plasma and extracellular calcium concentrations is limited by a high phosphorus concentration. The plasma and extracellular calcium concentrations determine the amount of calcium transported across the cell membranes of the parathyroid gland, and this controls the synthesis and/or secretion of the hormone. There is little evidence that a trophic effect is exerted by the pituitary or that any influences other than calcium levels control parathyroid secretion. The suggestion has been made that hyperparathyroidism may have its origin in previous hypocalcemia which causes increased parathyroid activity and eventual adenoma formation or autonomous hyperplasia. Pancreatitis is occasionally accompanied by low plasma calcium concentrations, and it has been suggested that pancreatitis may be such a stimulus; but there is little evidence to support this belief.

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Clinical Manifestations

There are seven clinical modes of presentation of hyperparathyroidism, but only two are common. 1. *Renal calculus formation* occurs in about 70% of cases and develops primarily because of the presence of high urine concentrations of calcium. There is some evidence that a second factor may also promote renal calculus formation. When bone resorption occurs, not only is calcium released but bone matrix is destroyed. Mucopolysaccharides and glycoproteins similar to those found in bone matrix appear in the urine in hyperparathyroidism, and there is evidence to suggest that these may cause nucleation and, eventually, calculus formation. Occasionally, the urine calcium is not high in hyperparathyroidism; when it is not, renal calculus formation usually does not develop. If renal insufficiency has occurred, the filtered load of calcium may be normal or subnormal. In other cases, since the hormone increases tubular reabsorption of calcium, the excretion of calcium may be normal even if the filtered load is high.

2. A second common mode of presentation of hyperparathyroidism is illustrated by today's patient. *Upper gastrointestinal symptoms* occur in about 25% of cases. About 10% have peptic ulcers and about 5%, pancreatitis. An additional 10% have symptoms suggestive of one or the other, but no gastrointestinal pathology can be demonstrated. The cause of an increased incidence of peptic ulcer in hyperparathyroidism is unexplained. As for the pancreatitis, ductal calculi are common in patients with coincident hyperparathyroidism and pancreatitis, and possibly increased amounts of calcium are secreted by the pancreas with the development of calculi and reflux pancreatitis. A second possibility is that calcium, as an activator of trypsin activity, may cause intracellular activation of trypsin with a resultant pancreatitis.

The five remaining modes of presentation are rare. 3. These include the development of *bone manifestations such as pain, pathologic fractures, giant cell tumors and bone cysts;* the osteitis of hyperparathyroidism. 4. *Neuromuscular symptoms such as fatigue, lethargy, psychosis or coma may develop.* Calcium is a stabilizer of neuromuscular cell membranes, and with high plasma calcium concentrations, a considerable diminution in neuromuscular irritability may be present. 5. *Polyuria and polydipsia* may occur, due to an inability to concentrate the urine. 6. *Renal insufficiency* may appear, due to nephrocalcinosis. The nephrocalcinosis may not be obvious by x-ray, and microscopic nephrocalcinosis can cause extensive renal damage. 7. *Hypertension* is present in 50 to 70% of patients with hyperparathyroidism but is only rarely the presenting symptom. In about half the patients who have hypertension and hyperparathyroidism, there is sufficient renal disease present to explain the increased blood pressure. In the remainder, it has been suggested that a calcium-mediated increase in vascular smooth muscle tone is involved. Calcium is not only a stabilizer

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of neuromuscular membranes but a direct stimulator of muscular contraction.

Diagnosis

The diagnosis of hyperparathyroidism requires three criteria: 1. the presence of a proper clinical setting: at least one of the seven described and preferably one of the first two; 2. hypercalcemia, either persistent or transient; and 3. elimination of other causes of hypercalcemia. On rare occasions, patients with proven parathyroid adenomata have not met all three criteria. The one that is usually not present is hypercalcemia. The present patient's plasma calcium fluctuated between 12.5 and 16 mg.%. If a lesser degree of hyperparathyroidism were present with a maximum plasma calcium of 13 mg.%, fluctuation between 10 and 13 mgm.% could have occurred. If one were so unfortunate as to evaluate such a patient at the wrong time, diagnosis might prove difficult. If renal disease has intervened, not only may urine calcium excretion be diminished, but plasma calcium concentrations may decrease as the serum phosphorus rises due to phosphate retention. It has also been suggested that some of these tumors might secrete calcitonin as well as parathyroid hormone and the two counteract each other with regard to plasma calcium levels. However, this possibility is highly speculative.

Dr. Michael Golding*

Nonparathyroid tumors have been implicated in high blood parathormone levels. What is the incidence compared with primary parathyroid gland involvement and when should one search for these as the cause of hypercalcemia?

Dr. Irving Enquist**

I would say that any of the extracervical tumors that elaborate parathormone are quite obvious and therefore should be detected by a good work-up. They are usually renal, pulmonary, retroperitoneal, adrenal, or of unusual types. I think their incidence is much less than primary parathyroid tumors as a source of elaboration of parathormone.

Dr. Henry Schnitman†

In the case presented, do I assume correctly that it was a large adenoma?

Dr. Richard Rosen

Well, it's a matter of interpretation. There was one very large adenoma and there was another enlarged parathyroid which might have been an adenoma. There were also normal parathyroids.

Dr. Schnitman

This fact confuses me. Usually, when you find one adenoma, the other glands are hypoplastic.

Dr. Enquist

I feel the same way Dr. Schnitman does. If you have an adenoma, the remaining glands should be normal and small. Logic supports this. However, we recently had a patient whom we explored and in whom we found one perfectly normal gland. A second gland was large, and we thought it was an adenoma until Dr. Minkowitz found it on frozen section to be full of fat. Finally we found another parathyroid gland which we removed and which was in fact an adenoma, no more than 5 mm. in maximum size.

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The Tobacco Tyrant*

Witthaus & Becker's Toxicology reports: "Tobacco enemata were formerly frequently used, and have caused a number of poisonings, several of which have resulted fatally. Severe and even fatal poisonings have been caused by administrations and decoctions of infusions of tobacco "pipe oil" by the mouth as popular remedies for various disorders, or to provoke abortion; by the use of food articles accidentally contaminated with tobacco; by water saturated with tobacco smoke given to a child to induce quietness; by chewers or "dippers" swallowing the juice; by children sucking foul tobacco pipes; by the application of tobacco to abraided surfaces, and even to uninjured skin; and by excessive smoking."

Osborne says: "The most serious disturbance caused by the abuse of tobacco is on the heart. While smoking may temporarily slow the pulse, soon, with a weak heart, the rapidity is increased and very soon the heart-action is frequent. While smoking, the blood pressure may be increased, with excessive use it is soon diminished. The heart may be irregular or intermittent, and there may be actual dilatation of the heart, and an insufficiency of the mitral valve, entirely due to the over-use and over-action of tobacco. Tobacco heart is recognized as a condition which can generally be cured by withholding tobacco."

Neuhof observed several cases of extrasystoles (usually auricular), one case of flutter, and one of fibrillation. He also reports in detail a case of sino-auricular block.

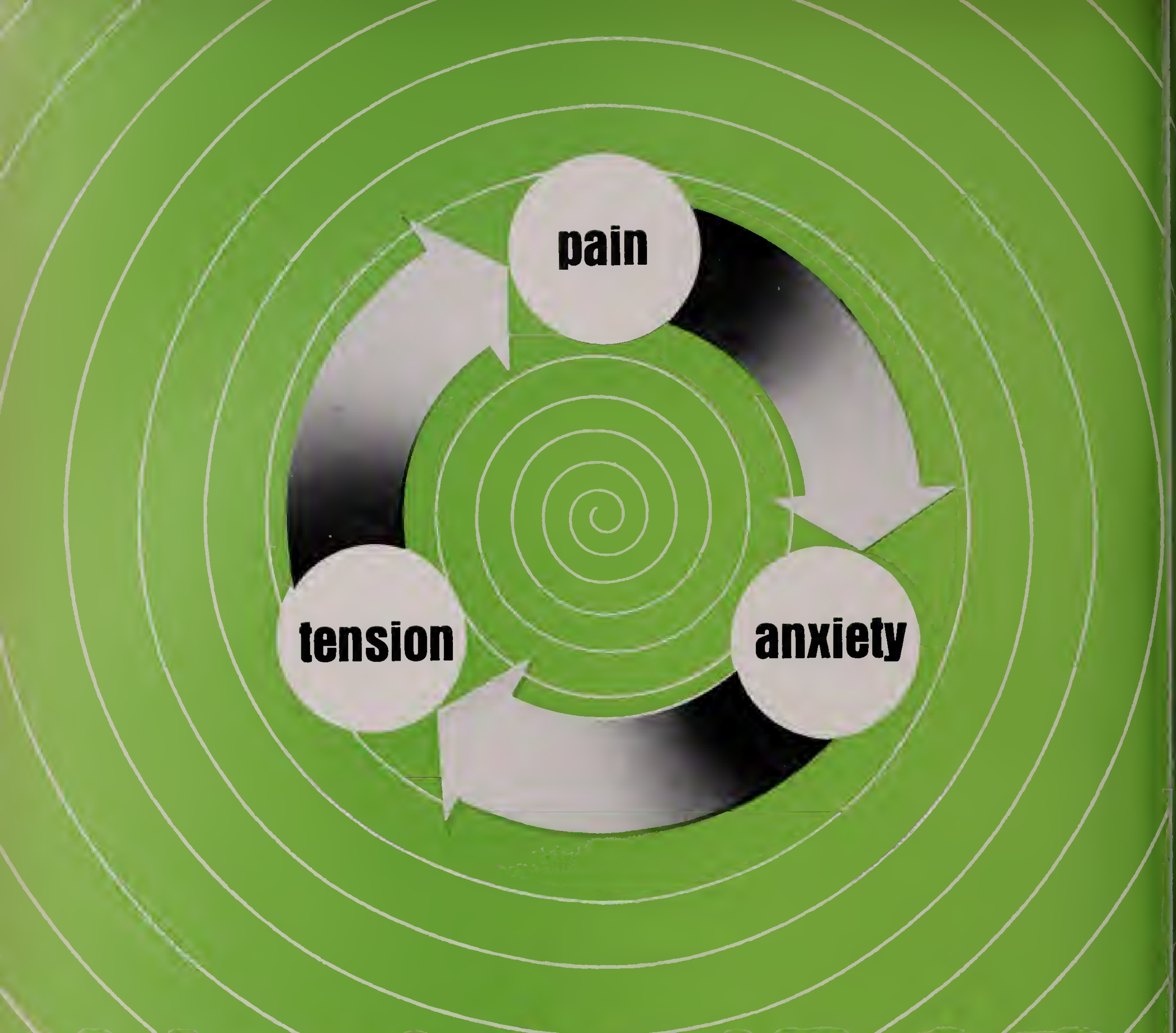
To be continued next issue.

E. O. Giere, M.D.**
Minneapolis, Minnesota

**Editor's Note: In 1928 Dr. E. O. Giere prepared and presented a manuscript at one of the Twin City hospitals on the evil effects of tobacco.*

***Through the courtesy of his sons, Doctors Richard and Joe Giere, the timeworn and faded manuscript was made available to the editor. Excerpts will be printed serially.*

See Minnesota Med 48:1376 and 48:1518, 1965.



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Grand Rounds

Pharmacotherapy of Sural Thrombophlebitis*

Since no thoroughly reliable means of prevention of venous thrombo-embolic disease exists, the major concern of the physician or surgeon remains the management of the established case and the prophylactic institution of therapy in those patients with known predisposition to venous thrombo-embolic disease. Until such time as the hospital laboratory can detect the presence of abnormal venous clotting, the appraisal and management of patients harboring venous thrombi must remain at the clinical level. Improvement in the use of present chief therapeutic methods, anticoagulant drugs, and venous division can result only from studies of treated cases, with particular emphasis on therapeutic failures.

Treatment

Before treatment is instituted the attending physician should have the goals of such therapy clearly in mind. These are:

1. Prevention of pulmonary embolization.
2. Prevention of clot propagation.
3. Prevention of chronic venous insufficiency.
4. Relief of the acute symptoms of thrombophlebitis.
5. Prevention of thrombus formation elsewhere.
6. Lysis of the thrombus already present.

Presently accepted methods of treatment utilize the following in attempting to fulfill the above goals:

1. General measures aimed at relieving acute symptoms.
2. Anticoagulant drugs
    a. Heparin
    b. Antiprothrombin agents
        1. Coumarins
        2. Indonedione compounds

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*The term thrombophlebitis as used in this presentation shall refer to the syndrome of a thrombus within the lumen of a vein with antecedent, concomitant or subsequent reaction of inflammation around and within the involved vein wall and thrombus.

Presented as a Medical Grand Rounds at Mt. Sinai Hospital, Minneapolis, May 25, 1965.

Continued

3. The use of fibrinolytic agents
4. The use of IV Dextran
5. Venous ligation in selected cases
6. Anti-inflammatory agents

General Measures

There seems to be almost universal agreement that general measures supplemented with one or more of the above specific measures have a definite and established place in any treatment program. These are utilized primarily to obtain relief of acute symptoms due to thrombophlebitis. They include bed rest, elevation of the affected extremity, local application of heat, and analgesics. In most instances, these are quite effective in relieving symptoms within 12 to 48 hours. Position in bed is important in promoting drainage of venous blood. The affected limb should be at a level higher than the thorax. Patients sitting with the head of the bed and affected limb elevated in the so-called "jack-knife" position have venous blood pooling in the pelvic veins, which may promote pelvic vein thrombosis. Local application of moist heat to a limb affected by thrombophlebitis aids in relief of pain and perhaps also by dilating the superficial venous system, thereby increasing the collateral vein channels. Analgesics such as aspirin, codeine and drugs of similar potency almost always suffice to relieve patients of discomfort.

Certain cautions are in order, however, when using the measures described above.

1. In patients with ischemic limbs and concomitant thrombophlebitis heat must be used with caution, if at all.
2. Elevation of an ischemic limb is usually contraindicated.
3. Drug and skin sensitivities must also be taken into consideration.

Anticoagulant Agents

Before the institution of anticoagulant therapy, it must be ascertained whether or not contraindications exist. These are listed by Estes as:

Absolute

a. Any blood dyscrasia which has purpura or hemorrhage as a manifestation.
b. Subacute bacterial endocarditis.
c. Recent brain or spinal cord surgery.
d. Recent major G.I. bleeding.
e. Laboratory facilities which are inadequate to provide accurate plasma prothrombin time determinations when the coumarins are used.
f. A physician who is untrained or inexperienced in anticoagulant therapy.

Relative

These situations call for increased caution and include the following:
a. Hepatic insufficiency.
b. Renal insufficiency.
c. Indwelling tubes (GU, GI, etc.)
d. Esophageal, gastric or duodenal ulcer, without recent bleeding therefrom.

e. Granulatory wounds, skin ulcers or potential bleeding sites.
f. Obstruction to biliary flow.
g. Severe nutritional or vitamin deficiency.

History

With the discovery of heparin by McLean in Howell's laboratory at Johns Hopkins University in 1916, there began a new era in the treatment of thrombo-embolic disease. Initially, heparin was only a research drug because of its impurity which caused severe reactions. Nearly 20 years passed before Best and his associates in Toronto produced a purified and concentrated product suitable for use in man. Clinical use of heparin began with the trials of Murray in Toronto in 1935 and with those of Crafoord in Stockholm in 1936. From this point on, heparin gained wide usage for the treatment of thrombo-embolic disease.

In the winter of 1921-22, veterinarians in the province of Alberta, Canada, and in North Dakota reported a new disease in cattle, "Sweet clover disease," characterized by excessive and sometimes fatal bleeding after trauma or surgery (castration, dehorning, etc.). In 1934, large scale experiments on the disease were initiated at the Wisconsin Agricultural Experiment Station under the direction of Link and Campbell and their associates. This work was greatly accelerated by the development of a quantative method for prothrombin determinations by Quick and coworkers. The active principle was finally obtained in pure form by Campbell and Link in 1941 and identified chemically as 3,3:methylene-bis (4-hydroxycoumarin), the only biscoumarin derivative found in nature. It is of interest that the same chemical had been synthesized by Onschutz in 1903. In 1934, Morawitz suggested that thrombosis could be prevented if a nontoxic agent could be found which would selectively and reversibly impair the production of prothrombin by the liver. Such an agent obviously had become available in bishydroxycoumarin. Meyer and Bingham and their co-workers at the University of Wisconsin and Butt and Allen and their associates in the Mayo Clinic conducted the first human experiments in 1941. Since this trial, these compounds have been extensively used in thrombo-embolic diseases.

The use of fibrinolysin, low molecular weight dextran, and anti-inflammatory agents is a fairly recent occurrence. Their value has not been fully demonstrated and they do not have an established place in the treatment of thrombo-embolic disease at present.

Mechanism of Action

Heparin

Heparin inhibits or prevents the clotting of blood both in vitro and in vivo. Therapeutic doses prolong the clotting time but do not affect the bleeding time. Heparin exerts at least four somewhat interrelated effects on the clotting mechanism of the blood:

a. It acts as an antiprothrombin to prevent the conversion of prothrombin to thrombin.

b. It quantitatively antagonizes thromboplastin by a mechanism not fully understood.

c. It prevents thrombin from reacting with fibrinogen to form fibrin.

Continued

d. It prevents agglutination of platelets, probably by preventing thrombin formation.

In addition to the anticoagulant properties, heparin possesses other actions. The most pertinent to this presentation is its anti-inflammatory effect.[1]

Coumarins

Bishydroxycoumarin affects blood coagulation by causing hypoprothrombinemia. The mechanism by which the compound inhibits prothrombin production has not been fully elucidated, but indirect evidence strongly suggests that it interferes with the role of Vitamin K in the liver synthesis of prothrombin. It is thought to produce this effect by competitive inhibition for the apo-enzyme essential for prothrombin synthesis.

Dextran

Dextran administered by intravenous infusion has been used by several investigators in molecular weights varying from 40,000 to 120,000. The proposed mechanism of action is threefold[3]:

a. It coats erythrocytes increasing the electronegativity of the cells and prevents sludging.

b. It coats the internal surface of vessels, decreasing the current of injury and thereby the agglutination of platelets at the site of internal damage.

c. It increases the peripheral blood flow.

Fibrinolysin

Commercial preparations currently contain both profibrinolysin (plasminogen) and an activator of streptokinase to bring about the conversion of plasminogen to plasmin.[4] Therefore, we don't really know if the foreign plasminogen is being activated or if the body's own fibrinolytic system is being stimulated. Clinical studies are few at present, with almost equal results using both in combination or streptokinase alone.

Anti-inflammatory Agents

Phenylbutazone is the only such agent frequently used in thrombophlebitis. It has no known anticoagulant effect and exerts only an analgesic, antipyretic action inferior to that of common aspirin.[1]

Clinical Studies

Sawyer[5] and associates conducted a study to compare the effects of conservative management, heparin therapy and fibrinolysin therapy. They had a total of 43 patients with acute sural thrombophlebitis. Selection of patients for therapy was done by randomized envelopes. Usual historical and physical findings supplemented with immediate bilateral phlebography were used for diagnosis. Patients were excluded from the study if they had had symptoms for longer than 48 hours.

Patients in Group A received only symptomatic treatment, plus penicillin (1 million units twice a day) and streptomycin (0.5 gm. twice a day). Group B received, in addition, heparin intravenous 50-75 mg. every four hours. Group C received 50,000 to 100,000 units of intravenous Thrombolysin (plasminogen and streptokinase) every two hours.

Patients in Group B had a significantly more rapid symptomatic recovery than those in either Group A or C. There was no pulmonary embolization in Group B but two deaths in Group A and three in Group C from pulmonary emboli.

It was not possible to use days of therapy to ambulation and discharge because of an obligatory 12 to 14-day bed stay before post-treatment phlebograms could be performed.

Seven hundred and forty-four (744) cases of thrombo-embolic disease, occurring over a 10-year period at the Massachusetts Memorial Hospital, were reviewed.[6] Patients were randomly selected and treated with heparin alone, intramuscularly, intravenously or subcutaneously, bishydroxycoumarin alone, heparin and bishydroxycoumarin. The authors conclude that intermittent intravenous heparin therapy carried out for a minimum of 10 days is the treatment of choice. Dicumerol appears to have little to offer in the therapy of the acute case from the standpoint of prevention of pulmonary embolization, prevention of recurrence of thrombotic process, or speed of subsidence of the inflammatory process.[7,8]

Carey and Williams[9] produced experimental thrombi in dogs by applying a small direct current to the surgically exposed external jugular vein. They concluded that propagation is prevented if the Lee White time is 1½ pretreatment value. Propagation was not prevented by dicumerol or tromexon unless prothrombin time values well below 20% were maintained.

Since October 1, 1940, 947 cases of deep venous thrombosis have been treated with intermittent intravenous heparin at the General Hospital in Mariestad, Sweden.[10] The patient was not disturbed at night, and no Lee White clotting times were performed. This dosage was continued until the patient was free from thrombophlebitis symptoms (average 4.42 days). He was then given 150 mg. of heparin and ambulated. If no recurrences of symptoms occurred during ambulation he was treated for an additional day and allowed to leave the hospital wearing an elastic stocking on the affected leg. In the entire series, the incidence of pulmonary embolization was 0.9% with seven deaths. There was a recurrence rate of 2.4%. A slight hemorrhagic tendency was observed in only 14 cases (a rate of 1.5%). None of these patients required more therapy after withdrawal of heparin.

Studies by Moncrief[3] and Cox et al. with dextran appear to be very promising but are presently very limited and still at the experimental stage.

Conclusions

There seems to be general agreement that intermittent intravenous heparin is the drug of choice in the treatment of acute sural thrombophlebitis. Although some will object to the cost of heparin (average $10 per day), the money saved the patient by reduced hospital stay and decreased incidence of complications will more than offset this objection. From the current work being done with dextran, this appears to have the

Continued

potential of replacing heparin as the drug of choice. However, more clinical studies will have to be performed in order to accomplish this.

Roger Schroeppel
Medical Student Extern
Mount Sinai Hospital

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For Eye Disorders in Ancient Egypt

The Ebers Papyrus of ancient Egypt dealt comprehensively with diseases of the eye; from blepharitis to trichiasis; prescriptions for casual and minor eye disorders abounded.

For bleary eyes an extraordinary concoction of onions, myrrh, verdigris, cypress-from-the-north, antelope dung, oil, and entrails-of-the-qadit-animal was recommended — to be painted on the eye with a vulture's feather. Since, however, antelopes, qadit-animals, and vultures were beyond the financial reach of most Egyptians — pharaohs and plutocrats excepted — the proletariat could substitute the lowly, versatile, and ubiquitous ass. In fact, just one ass's tooth alone would avail — provided it was well-wet with water and applied all around the bleary eye.

For bloodshot eyes one remedial procedure consisted of alternately bathing the eyes in two separate mixtures: one consisting of Fruit-of-the Dompalm and Milk-of-a-Woman-who-has-borne-a-Son, and the other — anticlimactically — of Cow's Milk.

Squinting was overcome by applying a salve of equal parts of Tortoise-brain and abra-ointment.

Hot eyes could be relieved by mixing Tallow-from-the-Jawbone-of-an-Ass with Cold Water and applying it to the — temples!

Finally, Xanthelasma succumbed to a 50-50 compound of Red-lead and Goose grease smeared on the eyes, to which unique prescription the Scribe appended the rather cryptic exhortation: SEE TO IT!

As a man gets older, he suspects that nature organized him for the benefit of the dentists and doctors. — Anon

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To keep young, associate with young people. To get old in a hurry, try keeping up with them. — News Leader, Arcadia, Wisconsin

Collagen Synthesis and Lysis

in Healing Wounds

IRVING F. ENQUIST, M.D.*
ROLAND J. ADAMSONS, M.D.**
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THE MOST important biochemical change occurring in a healing wound is the synthesis and orientation of collagen fibers by fibroblasts. Production of collagen is the end result of a host of complex chemical reactions, many of which are little understood. Most attention has been directed at collagen synthesis and its subsequent maturation, and only recently has another aspect of collagen metabolism been recognized. It is now apparent that collagen is actively lysed during several phases of, if not throughout the healing process. Our purpose in this presentation is to summarize briefly the present knowledge of collagen synthesis and collagen lysis and their respective roles in the achievement of total wound healing.

Collagen Synthesis

Collagen Content vs. Tensile Strength

Dunphy and Udupa[1] measured the synthesis of collagen in granulation tissue of skin wounds in rats and related the concentration of collagen in these wounds to the tensile strength of healing, sutured skin wounds in different animals of the same species. During the lag phase the wounds showed no increase in collagen; but since there was a proliferation of fibroblasts and a marked increase in ground substance, Dunphy called this the "substrate phase." These changes were necessary precursors for those which immediately followed. With the end of the lag (substrate) phase the collagen content of the granulation tissue increased rapidly until the fifteenth day, at a rate very similar to the rate of gain in tensile strength of sutured wounds. These studies were done in normal animals.

Vitamin C Influence

Dunphy and his group[2] then showed further that Vitamin C deficiency resulted in a decreased collagen production in granulation tissue and that this corresponded to the known impaired healing of incised wounds in scorbutic animals. The direct relationship between collagen synthesis and tensile strength was thus established. However, Grillo and Gross[3] soon showed that contraction of open skin wounds in scorbutic animals was unimpaired. Also, in animals with alloxan diabetes Rosen and Enquist[4] found no impairment in the contraction of skin

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wounds, although the gain in strength of sutured wounds was markedly impaired. Both of these studies suggested that the mechanisms responsible for the healing of open tissue defects are different from those involved in the healing of sutured wounds. Therefore the study of the relationship of collagen to tensile strength will be more appropriately made if the two parameters are studied in the same wound.

With this background Rosenthal et al.[5] studied absolute collagen concentrations and tensile strengths of incised wounds in normal and alloxan diabetic rats. The wounds in poorly-controlled diabetic animals healed significantly more slowly than those in normals, but there was no difference in the collagen content of the wounds. Furthermore, Peacock[6] demonstrated that secondarily closed wounds healed faster than primary wounds of the same age, despite lower collagen concentrations. He postulated that although collagen is responsible for tensile strength, the biochemical and biophysical properties of the fibers are more closely related to tensile strength than are the absolute local concentrations. Gain in strength of wounds during the late or maturation phase is due to remodelling and increased cross-linking of collagen fibers, without any absolute increase in number.

Wound Collagen Excess — Positive or Negative

The studies cited above were made in small laboratory animals, all of whom showed marked and rapid changes in the collagen content of their musculature from any major stress — operation, bacterial infection, metabolic disorder, etc. The changes in muscle collagen under these circumstances are explained by a marked tissue catabolism leading to reduction of all cellular elements except the collagen framework, which then remains at a relatively higher local concentration. This is confirmed by the inverse relationship between body weight and muscle collagen seen in small laboratory animals after wounding. The total body collagen pool is apparently unchanged. For these reasons, examination of wound collagen *per se* is an inadequate indicator of collagen metabolism. The collagen concentration of a wound is a reflection of local collagen synthesis, local collagen lysis, and the changes resulting from systemic changes affecting the entire organism. To determine local collagen synthesis, one subtracts from total wound collagen the collagen concentration of unwounded muscle at a comparable region of the body. This difference is the "active" collagen, elaborated at the wound site for healing. We have labelled the fraction the "wound collagen excess."[7-9] When the "wound collagen excess" is positive, the wound is stronger than unwounded contralateral muscular wall; when the "wound collagen excess" is negative, the wound has negligible inherent strength. This is clearly demonstrated in healing incisions in normal and scorbutic animals and persists for about 15 days after wounding.

Collagen Lysis

In a a number of experiments we noted that healing, incised wounds were weaker on the third day than on the first or second days after wounding. Examination of collagen then showed that the wounds regularly — on the third day — contained less collagen than unwounded muscle; i.e., the "wound collagen excess" was negative. We postulated that active lysis of collagen was occurring on the third day, the end of the lag phase. Study of wounds during the late or maturation phase revealed the same phenomenon, but less pronounced. It is our view that the lysis of collagen during the lag phase involves old collagen already present in the tissues, but that the lysis occurring late is destroying newly-synthesized fibers.

Enzyme

Collagen has been considered a relatively nonreactive protein participating slowly in the body metabolism; but it is now obvious that the enzymes capable of breaking down collagen had to be present in the tissues. Decrease of collagen has been shown in areas of granulomatous inflammation and in necrotizing skin inflammation produced by croton oil injection.[10] Lapierie and Gross[11] identified and measured a collagenolytic factor produced by the soft tissue in tadpole tail, and differentiated it from other proteolytic enzymes. Collagenolytic activity was also shown to occur in the metaphysis of long bones by Walker, Lapierie and Gross.[12] Activity was increased five to tenfold with parathyroid extract. Homogenates* of postpartum rat uteri contained five times as much collagenolytic activity as homogenates from nonpregnant uteri.[13] The discovery of this enzyme helps to explain the rapid decrease in the size of the uterus immediately post partum. Peacock[14] demonstrated nicely in his studies of the healing of tendon grafts that selective lysis and remodelling of deposited wound collagen played a vital role in the differentiation of scars, particularly in the restoration of gliding function in tendon grafts. He demonstrated microscopically the disappearance of fibrous adhesions and suggested that at some time during wound healing the production and lysis of collagen come into equilibrium. All of the work cited above gives adequate proof that collagen is readily lysed by mammalian tissues, and a number of our own studies lend support to this view.[7-9]

Inflammation

Because inflammation has been shown to cause lysis of collagen, and because catgut sutures are reported to cause a more vigorous inflammatory reaction than silk[15] we predicted that wounds closed with catgut would show a greater lysis of collagen than wounds closed with silk. However, under the ideal healing conditions of our experiment, we found no difference in collagen lysis between the silk and catgut wounds.[7] We therefore concluded that the amount of tissue in the inflammatory reaction about the sutures was insufficient to affect collagen lysis. It must be emphasized that this observation is valid only for wounds healing under ideal conditions and is not applicable to wounds with impaired healing.

Collagen lysis during the lag phase is seen in only a very narrow zone along the incision, with maximal collagen resorption occurring in the area between the incision and 1.85 millimeters away.[9] On the third day this narrow strip contains 89% of the collagen present at the time of wounding. In the next zone (1.85 to 3.7 mm. from the incision) lysis of collagen is less active. We have no knowledge if these changes which occur during the lag phase are also occurring throughout the healing period; however, during the later stages (after the tenth day in rats and after the ninth day in guinea pigs) decrease in wound collagen concentration has been noted.[5,8,9] Although the lysis of collagen during the lag phase affected only the narrow zone about the wound, the lysis noted later is evident throughout the biochemically active zone of the wound; in the guinea-pig musculofascial wall it was seen as far as 7.4 millimeters from the wound proper. Also, the balance between collagen synthesis and lysis is more homogeneous, resulting in a wider reactive zone in which the collagen concentration and collagen orientation are more even throughout the zone and there is maximum tensile strength per unit area. In scorbutic guinea pigs collagen lysis was much more marked and more prolonged. The lowest wound collagen was measured five days after wounding and only by the fifteenth day had the wound regained the collagen concentration of normal tissue.[8]

Recently Grillo and Gross demonstrated collagenolytic activity in the margins of open skin wounds in rats from 48 hours after wounding until the wound was healed.[16] Both epithelial and mesenchymal elements were required. However, in our studies collagen lysis was clearly observed in musculofascial wounds where epithelial elements could not participate. This is not easily explained, but the mechanisms of collagen lysis may be considerably different in sutured and open wounds.

Lack of Healing and Wound Disruption

A slight decrease in tensile strength of sutured wounds during the lag phase has been observed by Fast, Nelson, and Dennis[17] and by us.[8] This decrease parallels the collagenolytic activity of the wound. Excessive collagen lysis may be one of the factors responsible for decreased strength in sutured

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*See Test Your Word Score Page 1639.

wounds or even for frank wound disruptions. It is our opinion that *lack of healing* and *wound disruption* may be due to different and unrelated processes. *Lack of healing* means absence of collagen synthesis, whereas decreased tensile strength in a wound is a result of the lack of collagen synthesis and the increase of collagen lysis. In some situations collagen synthesis may be adequate; but the new collagen may be so actively lysed that none is present, leaving the wound without strength. Also, the reverse is true. In truly scorbutic animals there was no collagen synthesis in sutured incisions for a period of 15 days;[8] however, none of these wounds disrupted. We believe that the explanation for this is the near absence of collagen lysis in the wounds, leaving the old established collagen fibers undisturbed. With the sutures in place these wounds could hold; however, when they were tested after removal of the sutures there was absolutely no breaking (tensile) strength. We believe that in some clinical situations collagen synthesis proceeds normally but is outstripped by a very active collagen lysis which then destroys old and new collagen, leaving the wound markedly deficient in collagen and susceptible to wound disruption.

Summary

Collagen synthesis is the ultimate achievement of the chemical changes occurring in a wound and is responsible for the wound's strength. From many sources, evidence is now being presented to suggest that lysis of collagen is widely encountered and is an essential aspect of normal wound healing. A balance between collagen synthesis and collagen lysis must be achieved. When defective healing is encountered, the balance has been disturbed: there is either insufficient synthesis or excessive lysis. Finally, the spectrum of collagen chemistry in open wounds may be vastly different from that observed in closed, sutured wounds.

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9-17 May be secured from the author or the reprints.

Experitissimum

Experitissimum was Gilbert of England's magical formula for treating epilepsy in the thirteenth century: At the first access of the disease, when the patient falls to the ground, all his clothes except his shirt should be removed and placed at his feet. The nails of all his fingers and toes should next be clipped and wrapped in a cloth. A long white thorn is then to be split and the patient dragged feet first through the cleft as far as his middle. The thorn should then be cut into bits and placed with the nail parings. Next the patient's hair should be cut in three places. These clippings of hair and the knife used in the operation are then to be added to the other paraphernalia wrapped in the cloth, and the whole is to be buried underground, and the following words uttered. In the patient's right ear, "Christ conquers"; in his left ear, "Christ reigns"; and to his face, "Christ commands."

Lynn Thorndike in A History of Magic and Experimental Science.

Abstracts, Briefs and Commentaries

EXTENSION-FLEXION NECK STRAIN

"Whiplash" is not a good term, as there is no seven-pound weight on the end of a whip. The injury has been noted for thousands of years. The present cause of most of these injuries is a rear-end auto collision, with the recipient in a relaxed position.

The term "whiplash" indicates ligamentous injury in an area where ligaments are many and intricate. Bony injuries and ligamentous tears may be revealed by x-ray. Prolapsed discs have been diagnosed. The torn ligaments of the cervical spine are compared with those of a sprained ankle which may not heal well, leaving a relaxed joint. The symptoms due to trauma may be severe, resulting in headache, paresthesia, muscle spasm, and pain.

The majority of the injuries involve the lower cervical spine. High spinal involvement may cause subluxation with referred pain along the occipital nerves. Prolapsed discs have been reported in 26 per cent of patients with cervical sprain; but this is not the experience of the authors. Vague symptoms of blurring vision, diplopia, vertigo, nausea, etc. have been attributed to injuries to such structures as the vertebral arteries and to the vascular supply to the cord.

Initial treatment consists of adequate immobilization of the neck by a cast or Peterson brace. Hospitalization may be advisable. Traction is not recommended. Heat, relaxants, and sedation may be indicated. Immobilization of the neck is instituted for at least six weeks. Many patients continue to have symptoms after removal of the brace and require further treatment, such as steroid injections of trigger points. However, the authors believe that 80 per cent of patients lose their symptoms within one year.

From 1956 to 1963 more than 10,000 patients with neck pain were seen at the Mayo Clinic. This report is not concerned with patients operated upon for discs or fractures due to trauma involving the neck, but with 32 patients with cervical sprain that required fusion. These operations were determined by a history of severe trauma, persistent for one year or more; surgery was also resorted to in cases where symptoms, relieved by four weeks of immobilization, returned after removal of supports.

All 32 patients had severe accidents, 23 in rear-end collisions. An average

Continued

of 28.3 months elapsed between the accident and the operation. The trial brace relieved the pain and showed the patient what he might expect from surgery. All 32 patients had recurrence of symptoms after the trial immobilization.

Surgical treatment consisted of fusion of the lower cervical and upper thoracic vertebrae by bone grafts. Marked mobility of the spinous processes, laceration of some of the interspinous ligaments, with calcium deposits and tissue degeneration, were found at surgery.

Postoperative results are divided into four groups based on signs and symptoms. Among 31 patients followed none were the same or worse than before surgery; 64.5 per cent had excellent results; 25.8 per cent good results; and 9.7 per cent only fair results.

The authors also discuss the history, causes, and prevention of neck injuries.

Comments: This report is most interesting and timely, as it deals with a field often lucrative to the malingerer and his attorney, and a pain in the neck to the physician. Whether true or false, subjective symptoms are hard to classify. The authors note that some patients get relief when their claims are settled, as was the case in the so-called "railway spine." The review is excellent and based on extensive personal experience.

Stanley R. Maxeiner, Sr., M.D.
Minneapolis, Minnesota

Janes, Joseph M., and Hoosmand, Hooshaug: Severe Extension-Flexion Injuries of the Cervical Spine. Proc Mayo Clin May, 1965.

FOOD ALLERGY

The diagnosis of food allergy should be reached by using one or more diagnostic procedures, since no single method is totally accurate. First, one should try to establish the existence of food allergy in the patient; and second, one should attempt to identify a specific food as a cause of symptoms. If skin tests are used, they should be employed in the light of their limited value. They are never to be used alone, but should be supplemented in every instance by other diagnostic measures. Diets are featured by the omission of one or more of the most common allergens. When the patient is freed of symptoms, then the individual foods are checked in order to make the specific diagnosis. The deliberate feeding test, which is slow but highly accurate, requires the absolute cooperation of the patient in eliminating the food to be tested for four days. Only one food can be tested each day, which makes the diagnosis a prolonged procedure. In light of present knowledge, the provocative food test seemed safe, comparable in accuracy to the feeding test, with the advantage of making possible several tests in one day. Statistically, the authors have analyzed the time of reaction, the common neutralizing dilutions, and the comparative value of the deliberate feeding test.

Courtesy of References and Reviews
Journal of the American Medical Association

Rinkel, H., and Willoughby, J.: Arch Otolaryng 79:71, 1964.

VENOGRAPHY OF LOWER EXTREMITIES

One hundred and six venograms of the lower extremities were performed in 77 patients. Venography was employed to aid in diagnosis in clinically equivocal thrombophlebitis to diagnose previous disease of the deep veins, to evaluate thrombolytic therapy, and to study the natural history of thrombophlebitis. Thirty patients were examined because of suspected thrombophlebitis, but the diagnosis was radiographically confirmed in only two. Of nine patients with a history of previous phlebitis or with unexplained swelling, deep venous obstruction was present in only two. In 27 patients in whom serial venograms were made to evaluate fibrinolytic therapy, some lysis was observed in 9. The examination is easy to perform and complications are minor and infrequent. Venography of the lower extremity is a valuable adjunct in the examination of the deep veins of the lower extremity, because the deep veins are often difficult to evaluate clinically, and bedside examination is often inconclusive or misleading.

Courtesy of References and Reviews
Journal of the American Medical Association

Kramer, R., Weigen, J., and Hecker, S.: Ann Intern Med 59:798, 1963.

ALCOHOL-PANCREATIC DUCT

Clinical evidence indicates that alcohol is important in the pathogenesis* of pancreatitis. Researchers suggest several ways in which the alcohol works: 1, it acts directly on the cells of the pancreas through the blood stream; 2, duodenal congestion produces obstruction of the ducts; or 3, persistent vomiting causes regurgitation of duodenal contents into the ducts. Acute pancreatitis has frequently been observed to follow overindulgence in food or alcohol. The mechanism was thought to be rupture of the smaller ducts due to increased pancreatic duct resistance. Hemorrhagic pancreatitis has been produced in dogs by the intravenous injection of secretin after ligation of the ducts.

The authors studied several procedures after the main-duct catherization to accurately record intraductal pressures. Intravenous injection of secretin produced a prompt rise in intraductal pressure associated with active construction of the pancreatic duct papilla. Morphine injected intravenously produced a rise of intraductal pressure about twice that of secretin. Intravenous alcohol produced no elevation of pressure; but duodenal instillation of 20 cc. of 10 per cent alcohol increased the pressure to about half that of secretin. The instillation of 20 cc. of 20 per cent alcohol into the duodenum produced a similar response which lasted about twice as long.

The investigators concluded that secretin, morphine, and alcohol increased intraductal pressure, but that alcohol was effective only when introduced into the duodenum.

Comments:

A patient of ours who was unaccustomed to the use of alcoholic drinks had an attack of pancreatitis following a moderate amount of wine, and one year later he had a similar attack after drinking wine at a family anniversary. Following the second attack we performed a plastic operation on the ampulla with no subsequent reported recurrence.

Stanley R. Maxeiner, Sr., M.D.
Minneapolis, Minnesota

Walton, B. E., Shapiro, H., Yeung, T., and Woodward, E. R.: Effect of Alcohol of Pancreatic Duct Pressure. Amer Surg 31:2, 1965.

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*See Test Your Word Score Page 1639.

STRABISMUS IN GENERAL PRACTICE

Great confusion reigns among the medical profession as to when a cross-eyed child should be referred to an ophthalmologist. This should be between six and nine months of age because visual and muscular coordinated reflexes, resulting in normal vision in each eye and in stereopsis, are developed at six months of age, and 80% are fixed by the age of two. Thus normal anatomic relations shortly after six months of age are necessary to avoid the formation of fixed, irreversible, abnormal reflexes leading to amblyopia and lack of stereopsis. It is emphasized that the insidious divergent strabismus must be treated in infancy in spite of apparent temporary improvement. It is suggested that among the reasons for delay in referring strabismus cases is the receipt of incorrect advice from the family doctor or from optometrists.

Courtesy of References and Reviews
Journal of the American Medical Association

Laws, H. W.: Canad Med Ass J 90:76, 1964.

EMOTIONAL PROBLEMS IN THE ADOPTEE

Comparisons were made between emotionally disturbed adoptees and emotionally disturbed non-adoptees in child and adult populations. Diagnostic categories were similar, but there were significantly higher percentages of aggressive and sexual behavior in the adopted child and of alcoholism and sexual behavior in the adopted adult groups. These symptoms appeared despite the fact that in over 60% of the subjects adoption had taken place prior to their sixth month of life. The greatest percentage of the group was reported as having no reactions to first being told of their adoption. Fantasies were reported about natural parents, leading in a number of instances to an active searching for them.

Courtesy of References and Reviews
Journal of the American Medical Association

Schechter, M. D.: Arch Gen Psychiat 10:109, 1964.

CORRECTIVE NASAL SURGERY IN CHILDREN

Obstructive nasal and septal deformities in children are usually traumatic and involve the cartilaginous septum and especially the caudal end of the septum. Surgical correction is required to avoid secondary facial deformities associated with chronic mouth breathing. Surgical treatment is conservative and is limited to previously injured tissues. The septum is transfixed and freed bilaterally. Pedicle grafts are formed from the deviated cartilage with minimal removal. Minor deformities of the external nose may also be corrected. The long term results demonstrate retention of the restored nasal airway and satisfactory development of the external nose.

Courtesy of References and Reviews
Journal of the American Medical Association

Jennes, M. L.: Arch Otolaryng 79:145, 1964.

CADAVER TRANSFUSIONS

Following the Russian lead, the authors show that cadaver blood can be successfully transfused from a suitable donor body, dead less than six hours, directly into a living recipient via a sterile rubber tube, using either a syringe and three-way stopcock or a simple closed pressure recipient tubing set with filter. They suggest the use of this method in battalion or regimental aid stations, field hospitals, base hospitals, or even in a foxhole on the battlefield itself. The dead man would simply be laid close to the soldier in shock and the transfusion proceeded with. Cross matches are not necessary. The surgeon or corpsman need take only a fleeting moment to check blood types listed on "dog tags" and proceed accordingly.

Courtesy of References and Reviews
Journal of the American Medical Association

Kevorkain, J., Nicol, N., Rea, E.: Milit Med 129:24, 1964.

SPONTANEOUS PNEUMOTHORAX

A review of 213 spontaneous pneumothoraces in 170 patients, over a 12-year period, is presented. Conservative treatment, thoracentesis, tube drainage, and pleural scarification are compared as to time, success of re-expansion, and complications of the treatment. Re-expansion was obtained in 54% of 92 pneumos with 26 days in hospital (no complications); in 38% of 103 pneumos treated with thoracentesis, 13 days in hospital (no complications); in 74% of 95 pneumos treated with tube drainage, 11 days in hospital (6 complications, 1 death attributable to treatment); and in 98% of 46 pneumos treated by major thoracotomy (43 with pleural scarification) and with 15 days in hospital (2 complications, 1 death). The authors' present policy of management of spontaneous pneumothorax includes: conservative management of cases with less than 10-15% collapse; initial thoracentesis in those with more than 15% collapse; tube drainage if thoracentesis does not hold the re-expansion obtained; in tension pneumothorax, tube drainage of those not immediately responding to thoracentesis; pleural scarification, usually with blebectomy, in those not expanded within 10 days with tube drainage, and in recurrent pneumothorax.

Courtesy of References and Reviews
Journal of the American Medical Association

Ransdell, H. T., and McPherson, R. C.: Arch Surg 87:1023, 1963.

STEROIDS IN HEPATITIS

The comparative effect of long-term steroid therapy on both hepatic function and pathologic changes was studied in a case of active chronic hepatitis. Steroids were withheld for short intervals during the period of study to determine the permanency of their effects and for purposes of control. The findings indicate that improvement in clinical well-being and in the results of biochemical tests may take place in the face of progression of the disease, as revealed in serial needle specimens of the liver. The observations leave open to serious question the effect of steroid therapy on the actual disease process of chronic hepatitis.

Courtesy of References and Reviews
Journal of the American Medical Association

Mistilis, S., and Schiff, L.: Arch Intern Med 113:54, 1964.

CLUBBING OF FINGERS

Clubbing of the digits, an unexplained sign associated with lung cancer, is diagnosed only if an altered angle between the nail and the finger exists.

Continued

The underlying process may progress to hypertrophic osteoarthropathy, with involvement of the periosteum and long bones. Clubbing associated with intrathoracic disease is best explained by a reflex increase of digital blood flow which originates in the thorax and is mediated through the vagus. Section of the vagus nerve can result in regression. Clubbing associated with extrathoracic disease remains unexplained, along with the observed changes in hormonal secretion, rouleaux formation in the blood, and the opening of peripheral and pulmonary vascular shunts. Multiple theories proposed previously are discussed, and caution is advised against the hasty acceptance of newer ones; the recent attempts to disassociate clubbing related to intrathoracic disease from hypertrophic osteoarthropathy remain premature.

Courtesy of References and Reviews
Journal of the American Medical Association

Just-Viera, J.: Arch Intern Med 113:122, 1964.

DREAMS

Psychodynamic investigation was made of 2 subjects' dreams experimentally obtained but not told to psychiatrist by the subjects in subsequent interview. Subject A reported to the experimenter dreaming on 34 of 46 awakenings, 7 being reported to therapist. Subject B reported to the experimenter dreaming on 54 of 60 awakenings of which 41 were reported to the therapist who explicitly asked for dreams. Dreams containing attitudes which the dreamer anticipates will bring forth negative response from the psychiatrist are not recalled. For men these were strong homosexual feelings. For women this was initially guilty sexuality and later on intense denial of dependency. Four additional factors influence the process of dream reports to the psychiatrist: (1) being awakened and immediately telling the dream; (2) interest of psychiatrist in dreams; (3) relationship between patient and psychiatrist at the time of the interview; (4) time of night of dreams, later dreams being better remembered than earlier dreams.

Courtesy of References and Reviews
Journal of the American Medical Association

Whitman, R., Kramer, M., and Bladridge, B.: Arch Gen Psychiat 8:277, 1963.

The hottest places in Hell are reserved for those who in time of crisis maintain their neutrality. — Dante

To keep his mind sweet the modern scientific man should be saturated with the Bible and Plato, with Homer, Shakespeare, and Milton; to see life through their eyes may enable him to strike a balance between the rational and the emotional, which is the most serious difficulty of the intellectual life. — William Osler

It is foolish to tear one's hair in grief, as though sorrow would be made less by baldness. — Cicero

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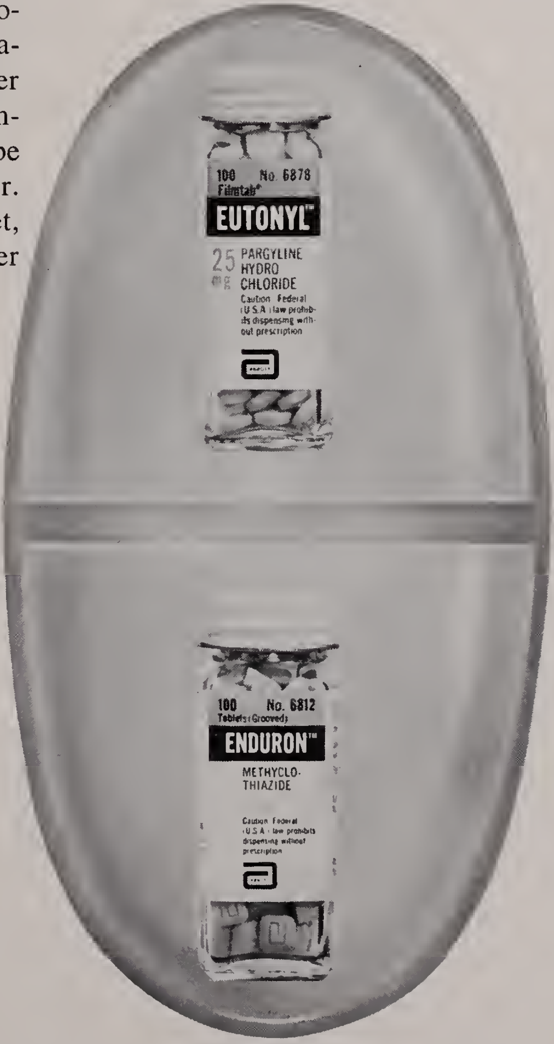
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1. Torosdag, S., Schvartz, N., Fletcher, L., Fertig, H., Schwartz, M. S., Quan, R. F. B., and Bryant, J. M., Pargyline Hydrochloride as an Antihypertensive Agent With and Without A Thiazide, Am. J. Cardiol., 12:822, Dec., 1963.

2. Pollack, P. J., Pargyline Hydrochloride and Methyclothiazide Combined In The Treatment of Hypertension, Cur. Thera. Res., 7:10, Jan., 1965.

3. Bryant, J. M. et al., Antihypertensive Properties of Pargyline Hydrochloride, New Non-Hydrazine Monoamine Oxidase Inhibitor Compared with Sulphonamide Diuretics, J.A.M.A., 178; 406, Oct., 1961.

BP reductions in the recumbent and sitting positions often are nearly as great as in the standing. In clinical trials, the average *recumbent* BP reduction was 36/18 mm. Hg.

The average *standing* reduction in clinical trials was 45/22 mm. Hg. Thus the difference between the standing and recumbent readings was only 9/4 mm. Hg.

Significantly lowers blood pressure in all body positions; less likelihood of orthostatic hypotension

In clinical trials, the average reduction in standing blood pressure was 45/22 mm. Hg.; in the sitting position it was 48/20 mm. Hg.; and in the recumbent position, 36/18 mm. Hg.

Because Eutron effectively reduces blood pressure in all body positions, there is reduced likelihood of orthostatic symptoms or hypotension.

This was reflected in the relatively mild character of side effects seen in clinical trials (see below).

Smooth and gradual onset

Onset of antihypertensive action is usually quite smooth. Initial reduction of systolic and diastolic readings is usually seen within a week – maximum reduction in seven to ten days.

Less troublesome side effects may be seen; frequent improvement in "sense of well-being"

Fewer than 1% of patients studied discontinued Eutron therapy because of side effects. This is due in part to the relatively low dosage needed with the combination. Usual recommended dose is one tablet daily–that is, 25 mg. Eutonyl with 5 mg. Enduron. *This is about half the usual therapeutic dose of Eutonyl given alone.* As a consequence side effects may be milder. And, as with Eutonyl given alone, the patient may well note an increased sense of well being. This is in distinct contrast to most other antihypertensive therapy.

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Prescribing information for **EUTRON**

INDICATIONS: Eutron (pargyline hydrochloride and methyclothiazide) is indicated in the treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. It is not recommended for use in patients with mild or labile hypertension amenable to therapy with sedatives and/or thiazide diuretics alone.

CONTRAINDICATIONS: Eutron is contraindicated in patients with pheochromocytoma, advanced renal disease, paranoid schizophrenia and hyperthyroidism. Until further experience is gained it cannot be recommended for use in patients with malignant hypertension, children (under 12 years of age), or pregnant patients.

The concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. A drug-free interval of two weeks should separate therapy and use of these agents.

WARNINGS: Pargyline hydrochloride is a monoamine oxidase inhibitor. Patients should be warned against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When it is necessary to administer alcohol, narcotics (notably meperidine), antihistamines, anesthetics, barbiturates and other hypnotics, sedatives, tranquilizers, or caffeine, these agents can be used cautiously at a dosage of ¼ to ⅕ the usual amount. Avoid parenteral administration where possible. Withdraw pargyline two weeks before elective surgery.

Patients should be warned about the possibility of postural orthostatic hypotension. Those with angina or other evidence of coronary disease should not increase physical activity. Pargyline may lower blood sugar. Potassium depletion is unlikely at the recommended dosage, but if it occurs, adjust dosage or withdraw or provide added natural food sources of potassium; potassium tablets should be avoided wherever possible, as bleeding or obstructive ulceration of the small bowel has been associated with their use; potassium levels should be especially watched if the patient is on digitalis or steroids, or if hepatic coma is impending.

PRECAUTIONS: When determining the antihypertensive effect of Eutron, blood pressure should be measured while the patient is *standing*. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Pargyline has not been shown to cause damage to body organs or systems. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. The drug should be used with caution in patients with liver dysfunction. With prolonged therapy, examine patients for change in color perception, visual fields, and fundi.

Elevated blood urea nitrogen, serum uric acid or blood sugar are possibilities attributable to the methyclothiazide in Eutron. Methyclothiazide may also reduce arterial response to pressor amines. Blood dyscrasias, including thrombocytopemia with purpura, agranulocytosis and aplastic anemia, have been seen with thiazide drugs.

SIDE EFFECTS: The use of pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extra-pyramidal symptoms have been reported. Drug fever is extremely rare. Congestive heart failure has been reported in a few patients with reduced cardiac reserve. Nocturia has been observed with the combination. If side effects persist, despite symptomatic therapy or reduction of the dose, discontinue the drug.

ABBOTT

512214

Book Reviews

Retirement without the love of letters is a living burial. — Seneca

HANDBOOK OF CLINICAL AND LABORATORY DATA AND PRACTICAL MANUAL FOR CLINICAL LABORATORY PROCEDURES (two volumes) — **First Edition. Editors: Henry C. Damm, Ph.D., and John King, M.D., Ph.D., The Chemical Rubber Co., Cleveland, Ohio, 1965. Price, $12.50 for single book, $22.50 for two.**

These companion volumes will serve as anchors for those who are being swept away by the tidal waves of the current medical literature. Using the format of *Handbook of Chemistry and Physics*, the editors bring together laboratory information in concise tables and brief discussions. Much of the data previously could be found only by foraging in dark corners of books and journals.

The board of editors, most of whom are associated with Western Reserve University or the Cleveland Clinic, have chosen contributors from both university and community hospitals. The result is a balanced, comprehensive presentation designed for physicians in active practice.

The material is wisely presented in two volumes. By not breaking the flow with interminable lists of methods, readability is achieved in the *Handbook* — a hardback compendium embracing most of clinical pathology. The material is introduced with early signs and symptoms of organ dysfunction, quickens with an appraisal of laboratory findings in related conditions, and culminates with a differential diagnosis.

The *Practical Manual*, on the other hand, is a looseleaf workbook with a straightforward "cookbook" presentation of methods. Included are procedures for blood banking, chemistry, hematology, histology, microbiology, and urinalyses. It will be a valuable source of lore for technologists and physicians who seek reliable, proven methods.

The uniqueness of the *Handbook* is its collection of useful data in an obtainable form. The pathologist can thumb to tables and discussions on such diverse but practical items as: dimensions and weights of organs in children and adults; proper handling and collection of bacterial specimens; automation, statistics, and quality control; toxicological techniques and absorption spectra of toxic compounds; and theories and procedures of immunohematology. The section on microbiology is refreshing — it has been shorn of oppressive minutiae. The clinician can fruitfully peruse "flow sheets" of endocrine function, assessments of acid-base balance, and a distilled critique of hematology.

My criticisms are minor and are counterbalanced by praise. The descriptions are scant, but the references are strategic. Some discussions, e.g., iron metabolism, are excessive, but this is compensated for by sinewy descriptions of other topics. The *Practical Manual* has neither a table of contents nor an index, but each section is separated by distinctive, easy-to-find colored pages — each with a list of contents of the section.

I recommend both volumes.

Richard L. Reece, M.D.
Minneapolis, Minnesota

OPHTHALMOLOGY PRINCIPLES AND CONCEPTS — **Frank W. Newell, C. V. Mosby Company, St. Louis, 1965. $12.25, 491 pages, 172 illustrations.**

This is a well prepared introduction to ophthalmology intended for the student. It would also serve well for the general practitioner or any other physician who wishes to have at hand a handy reference to the various ophthalmologic diseases. Bibliographical references are appended at the end of each chapter. For the specialist in ophthalmology the book would be didactic.

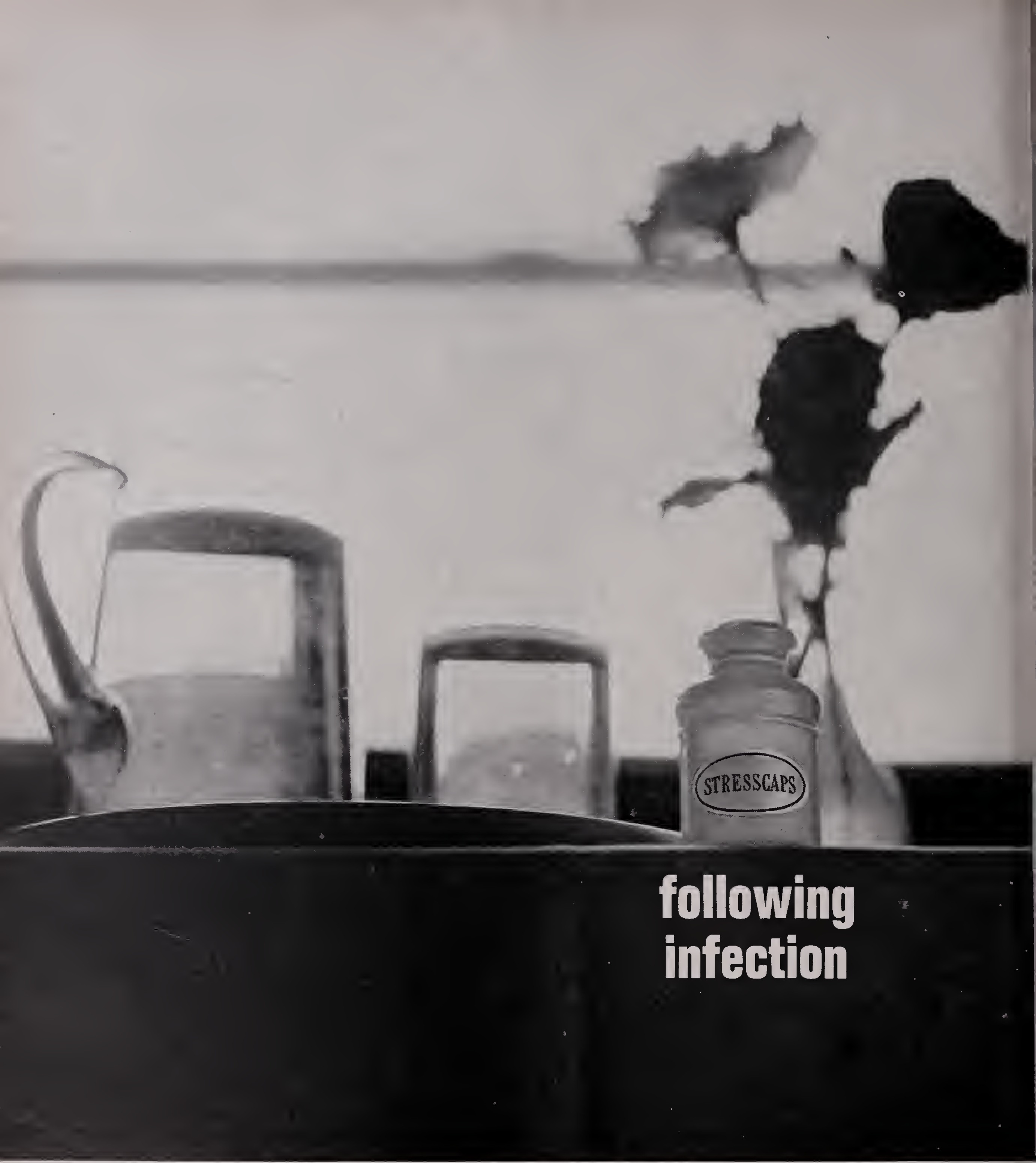
Carl O. Rice, M.D.
Minneapolis, Minnesota

MANAGEMENT OF THE PATIENT WITH SUBNORMAL VISION — **Gerald Fonda, M.D., F.A.C.S., C. V. Mosby Co., St. Louis, 1965. 161 pages, 88 figures, references, index, $11.00.**

This volume, written for the eye specialist, covers the application of various low visual aids to the needs of the partially sighted. The trend now is away from Braille and elaborate telescopic devices, which have been unjustly popularized, toward the use of strong convex lenses. These employ the principle of angular magnification in which regular print brought close to the eye is enlarged proportionally to the reduction in reading distance. In young persons the same effect can be obtained by using available accommodation which is not as commonly thought harmful. Of course, this does not improve distance vision and is not as useful in diseases characterized by marked reduction in visual field.

This book is well written, illustrated, and edited and fills a void in the literature.

William S. McClanahan, M.D.
Minneapolis, Minnesota



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Special Article

Some Reflections on Births and Infant Deaths among the Low Socioeconomic Groups*

EVELYN E. HARTMAN, M.D., M.S.**
ETHEL B. SAYLES, B.S.†
Minneapolis, Minnesota

MINNEAPOLIS AND environs constitute a medical center with a university medical school and hospital, a tax-supported county hospital, and nine private hospitals located within the City and three in outlying Hennepin County, all with maternity services. The number of private practicing physicians in Hennepin County is about 1,150, with a ratio of one physician per 730 population. The State ratio is one private practicing physician per 920 population. (Approximately 3,800 practicing physicians.)‡

The 1959 median family income in Minneapolis at $6,401 was well above both State and National figures (Table 1). The live birth rate in Minneapolis for 1961 and 1962, the resident live births in hospitals and the total number of live births to Minneapolis residents are also detailed in Table 1.

The prematurity and the illegitimacy rate are about the same as the national rate but above the State rate as illustrated in Table 2. Several social agencies located within the City provide care to unwed pregnant girls, attracting these girls to the City; this may account for the higher illegitimacy rate in Minneapolis.

The maternal, infant and fetal (20 weeks or more gestation) death rates in the City are about the same as State rates but considerably below national rates. The maternal deaths in the City from the medical standpoint are at an almost irreducible minimum. The only resident maternal death that occurred in 1962 was due to complications following abortion, either spontaneous or induced (unknown). The Minneapolis rates for perinatal mortality, which include fetal deaths at 20 weeks or longer gestation and neonatal deaths under 28 days of age, are about the same as the State rates, but well below the National rates.

From these statistics it would seem that the medical and hospital resources in Minneapolis are adequate and well utilized and that

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*Presented at Annual Meeting of American Public Health Association, New York City, October 1964.

**Director of Maternal & Child Health.

†Biostatistician.

‡Information from Minnesota State Medical Association and Hennepin County Medical Society.

Continued

the City is a safe place for expectant mothers to be delivered of their infants.

We were interested in determining whether or not these favorable rates were uniform throughout the City. If this was not the case, we wished to identify the problem areas and bring this information to the attention of responsible community groups, so that through the joint action of physicians, hospitals, and health and governmental agencies possible solutions to any problems of maternity care might be discussed.

Material

This study is based on collection and analysis of data from birth and infant death records for Minneapolis residents by census tracts; on social, economic and demographic characteristics of census tracts in Minneapolis according to the 1960 census; and on maternity patients at Minneapolis General Hospital in 1962. Included in this paper are:

1. Information on census tracts in Minneapolis with the lowest family income, lowest education, and highest unemployment, illustrated by maps.
2. Information on census tracts in Minneapolis with the highest birth, fertility, illegitimacy, prematurity, and infant death rates; with maps illustrating the areas in the City with the highest incidence of infant deaths and prematurity.
3. Comparison of the low socioeconomic areas in the City with areas having the highest birth, fertility, illegitimacy, prematurity and infant death rates.
4. Information on prenatal care for medically indigent patients attending the Minneapolis General Hospital in 1962.
5. Implications for community action.

Findings

Social, Economic and Demographic Characteristics

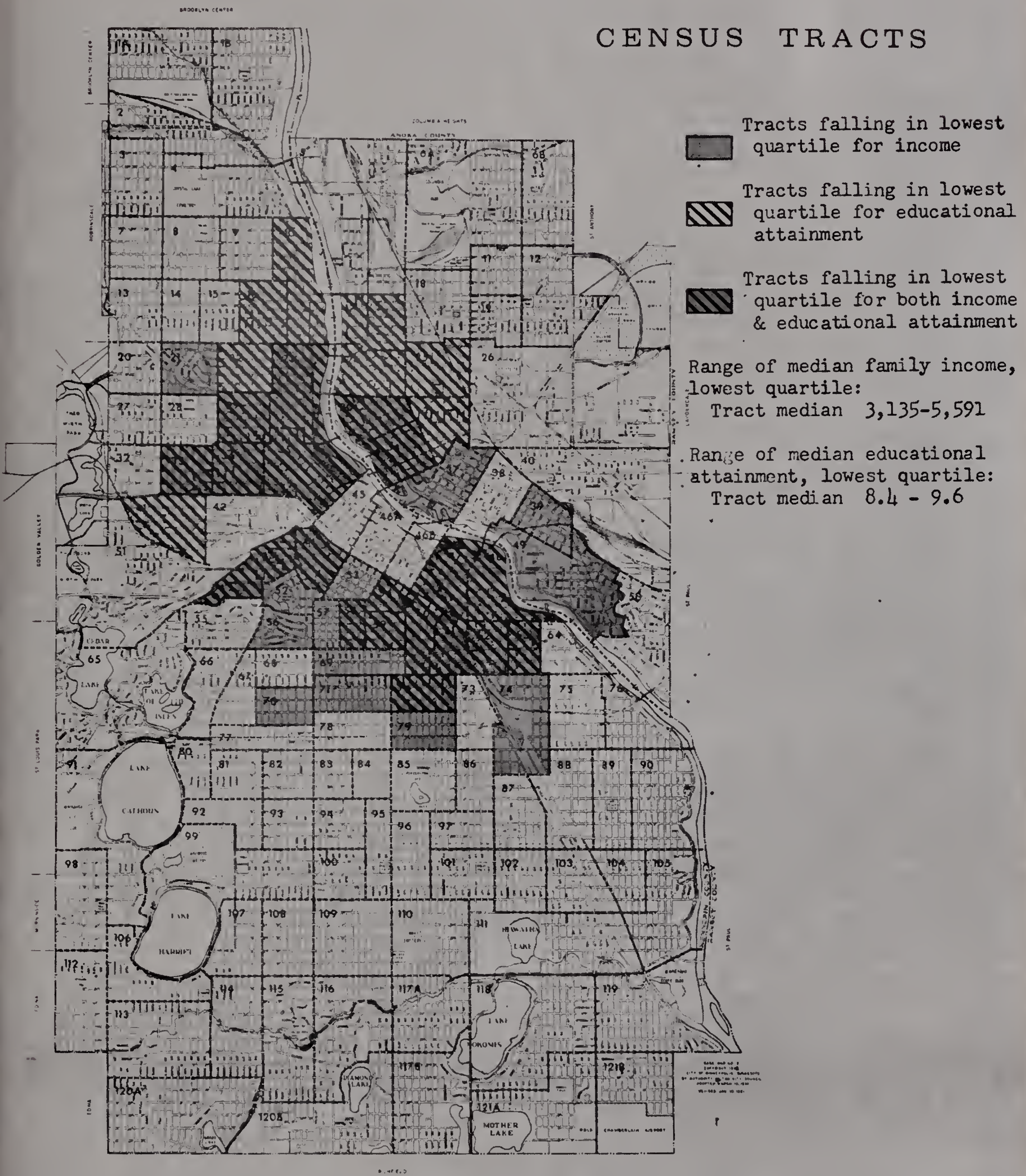
The median family income in Minneapolis (as shown in Table 1) is higher than in Minnesota and the United States. However, this is not uniform throughout the City,

TABLE I
Natality, Mortality and Income
United States, Minnesota, Minneapolis

	United States		Minnesota		Minneapolis	
Median Family Income-1959	$5,660		$5,573		$6,401	
Under $3,000	21.4%		21.4%		13.9%	
Over $10,000	15.1%		13.0%		17.3%	
	1962	1961	1962	1961	1962	1961
Live birth rate	22.4	23.3	24.3	25.0	23.3	23.2
Infant death rate	25.3	25.3	20.9	22.2	21.4	23.9
Fertility rate	112.1	117.2	131.7	134.1	111.2	112.0
Illegitimacy rate	—	22.6	16.6	15.3	—	22.6
Per cent premature (2,500 grams or less)	—	7.8	—	5.9	—	7.0
Fetal death rate (20 weeks or more gestation)	15.9	16.1	12.0	12.2	11.8	12.8
Neonatal death rate (Under 28 days)	18.3	18.4	15.7	16.5	15.5	18.2
Maternal death rate	3.5	3.7	0.1	0.2	0.1	0.3
Per cent of live births in hospitals	—	96.9	99.7	99.6	—	99.8
Illegitimate births per 1,000 live births	—	56.3	35.1	31.0	75 0	68.4
Perinatal mortality rate	34.2	34.5	27.7	28.7	27.3	30.9

Live Birth Rates — Live births per 1,000 population.
Infant Death Rates — Deaths under 1 year per 1,000 live births.
Fertility Rates — Live births per 1,000 female population age 15-44.
Illegitimacy Rates — Illegitimate births per 1,000 unmarried females age 15-44.
Fetal Death Rates — Fetal deaths (20 wks. or more gestation) per 1,000 live births.
Neonatal Death Rates — Infant deaths under 28 days per 1,000 live births.
Perinatal Mortality — Fetal and neonatal deaths per 1,000 live births.
Maternal Death Rates — Maternal deaths per 10,000 live births.
(—) Rates are not available.

Map 1. Correspondence Between Tracts with Low Family Income and Those with Low Educational Attainment, April 1960 Minneapolis, Minn.


CENSUS TRACTS
▨ Tracts falling in lowest quartile for income
▧ Tracts falling in lowest quartile for educational attainment
▩ Tracts falling in lowest quartile for both income & educational attainment
Range of median family income, lowest quartile:
Tract median 3,135-5,591
Range of median educational attainment, lowest quartile:
Tract median 8.4 - 9.6
LAKE CALHOUN
LAKE HARRIET
LAKE NOKOMIS
MOTHER LAKE
CEDAR LAKE
LAKE OF THE ISLES
ANOKA COUNTY
ST PAUL
GOLDEN VALLEY
ST LOUIS PARK

Source: Income, Education, and Unemployment in Neighborhoods
Bureau of Labor Statistics - U.S. Dept. of Labor .

Continued

with 13.9 per cent of families having an income under $3,000. The social, economic and demographic characteristics of census tracts, including median family income, white versus nonwhite population, median years of school completed, male unemployment, and median value of owner-occupied housing in Minneapolis according to the 1960 census vary considerably. Maps 1 and 2 show the census tracts in the City with the lowest family income, the lowest educational attainment, and the highest unemployment.

Although census tract 42 is not included on the 1960 map showing low family income, because public housing redevelopment was not completed in this area until 1962, a recent survey by the Minneapolis Youth Development Project has shown that the average family income at $3,700 places it very close to the bottom of the range.

Births, Infant Deaths, Illegitimate Births, Premature Births and Fertility

Table 2 lists in descending order the top ten per cent of Minneapolis census tracts for live births, infant deaths, illegitimate births, premature births and fertility in 1961.

Map 3 shows the census tracts in the City falling in the top ten per cent for infant mortality and prematurity in 1961. Census tracts 39, 43, 69, 95, and 107 are in the top ten per cent for both infant deaths and prematurity.

Census tracts 43 and 69 are in the top ten per cent for prematurity and infant deaths, as well as for illegitimacy.

Low Socioeconomic Census Tracts vs. Tracts Having Highest Rates for Natality and Infant Mortality

Census tracts 34, 42, 10 and 73 are in the top ten percentile for live births, illegitimate births and fertility. Public Housing Developments for low income families are in census tracts 34 and 42. Census tracts 10 and 73 are tracts having low education and high unemployment, and low income and education respectively. Although none of these census tracts is included in the top ten per cent for infant deaths and prematurity, in two of them the infant death rate was higher than the City rate of 23.9 and in three the percentage of premature live births was higher than the City-wide percentage of 7.0. The infant death rate for census tract 42 (for 1962) was 11.1 and the percentage of premature live births, 7.8. The infant death rates for census tracts 34, 10 and 73 (1961) were 46.4, 0.0, and 26.0 respectively; and 7.22, 5.05 and 9.09 per cent for prematurity.

Census tracts 39, 43 and 69 which were in the top ten percentile for infant deaths and

TABLE 2

Births, Infant Deaths, Illegitimacy, Prematurity and Fertility of Top Ten Per Cent of Minneapolis Census Tracts[1] — 1961

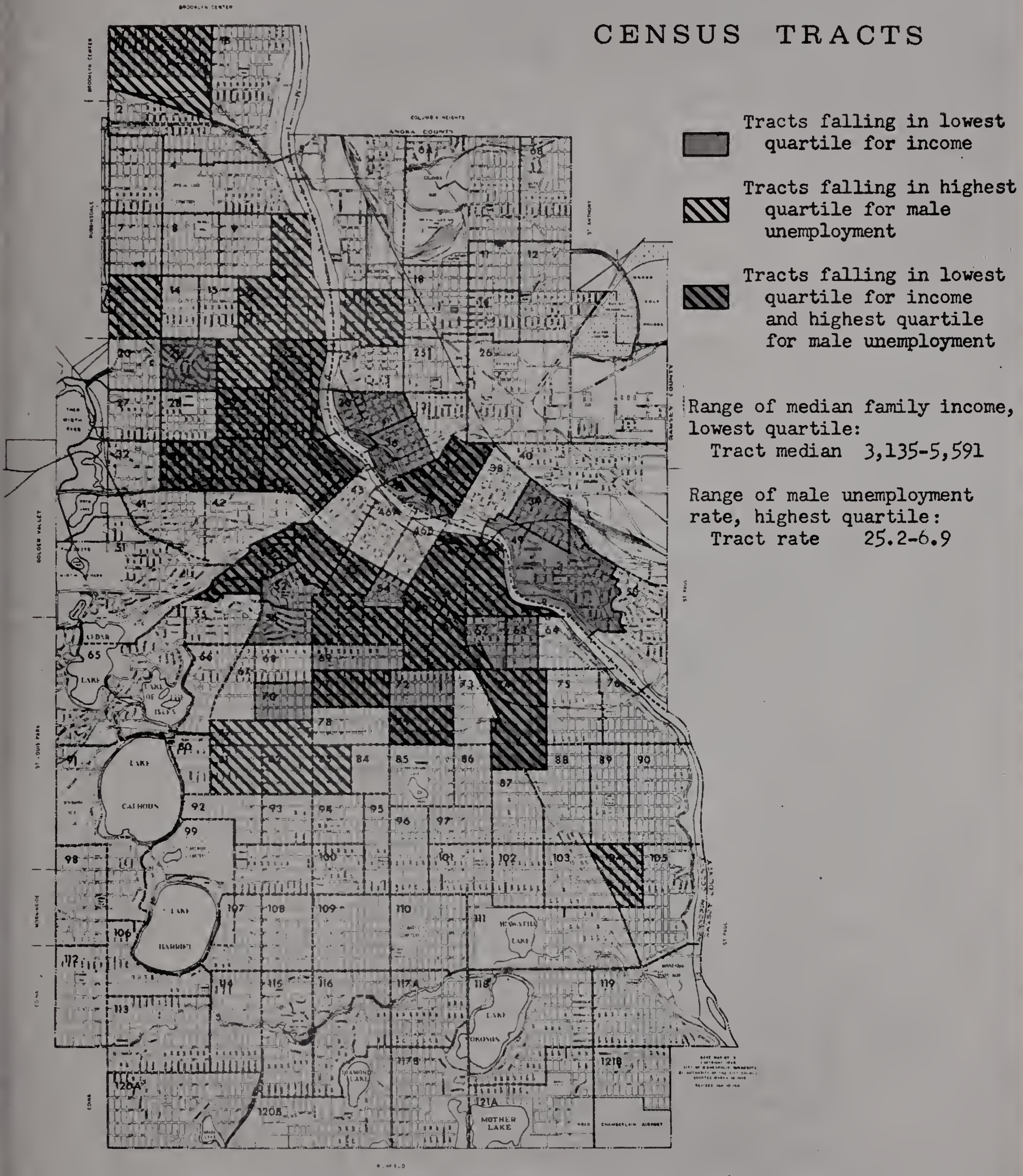
Live Births			Infant Deaths			Illegitimate Births			Premature Births[2]			Fertility	
C.T.	Number	Rate[3]	C.T.	Number	Rate[3]	C.T.	Number	Rate[3]	C.T.	Number	Per Cent	C.T.	Rate[3]
City	11,181	23.2	City	267	23.9	City	765	22.6	City	786	7.0	City	112.0
42	91	90.9	52	4	87.0	42	8	181.8	69	18	19.6	42	583.3
78	149	51.7	48	5	79.4	34	29	105.8	46B	3	18.8	34	206.8
34	194	40.5	43	3	76.9	33	21	98.1	43	7	18.0	26	188.3
26	138	37.2	107	4	69.0	47	9	92.8	39	7	15.9	10	187.6
10	100	37.1	39	3	68.2	35	9	90.0	29	17	15.7	31	177.2
63	86	37.1	69	6	65.2	43	9	74.4	9	13	14.3	47	176.8
73	77	37.0	62	5	62.5	100	9	66.2	37	11	13.3	73	176.2
31	140	36.5	118	6	54.1	61	14	58.8	47	7	12.7	17	175.7
40	227	36.1	104	3	50.0	69	17	57.6	95	11	12.5	79	172.4
82	158	35.3	120A	7	48.6	73	9	57.3	35	7	12.3	78	170.1
17	100	35.1	95	4	47.6	58	13	55.1	27	7	12.3	63	169.6
77	80	34.3	41	5	47.2	71	20	46.7	58	10	11.8	35	168.1
79	101	33.9	70	6	46.5	10	8	45.7	107	7	11.3	22	166.9

[1] Census Tracts 45 and 46A with less than 5 live births are omitted.

[2] Per cent premature based on live births occurring in the State. Information on prematurity is not available for births occurring outside the State.

[3] Birth rates per 1,000 population; infant death rates per 1,000 live births; illegitimate births per 1,000 unmarried females age 15-44; fertility rates — births per 1,000 female population age 15-44. U. S. Census of population — 1960.

Map 2. Correspondence Between Tracts with Low Family Income and Those with High Unemployment, April 1960 Minneapolis, Minnesota


CENSUS TRACTS
LAKE CALHOUN
LAKE HARRIET
LAKE OF THE ISLES
CEDAR LAKE
LAKE NOKOMIS
HIAWATHA LAKE
DIAMOND LAKE
MOTHER LAKE
ANOKA COUNTY
RAMSEY COUNTY
ST. PAUL

■ Tracts falling in lowest quartile for income

▨ Tracts falling in highest quartile for male unemployment

▨ Tracts falling in lowest quartile for income and highest quartile for male unemployment

Range of median family income, lowest quartile:
Tract median 3,135-5,591

Range of male unemployment rate, highest quartile:
Tract rate 25.2-6.9

Source: Income, Education, and Unemployment in Neighborhoods
Bureau of Labor Statistics - U.S. Department of Labor

Continued

premature births are also low for economic conditions. Infant deaths alone were high in the low socioeconomic tracts of 41, 48, 52, 62, and 70; and prematurity alone was high in the low socioeconomic tracts of 29, 35, 37, 46B, 47, and 58.

Infant deaths and prematurity in combination or separately were also high in the following census tracts in which the socioeconomic conditions were slightly lower than for the City as a whole: 9, 27, 104; and in the following census tracts in which the socioeconomic conditions were the same or higher than in the City as a whole: 95, 107, 118 and 120A.

Prenatal Care

About 10 per cent of Minneapolis births in 1962 occurred at Minneapolis General Hospital,* which is a resource for outpatient and hospital care for medically indigent patients meeting financial and residency eligibility standards, and for emergency care. In 1962 a total of 1,308 women delivered at the hospital. Of these, about 43 per cent had no prenatal care or made only one visit to the prenatal clinic. Of women attending the hospital prenatal clinic, about 3 per cent made their initial visit in the first trimester, 26 per cent in the second, and 71 per cent in their last trimester. Of the 1,032 women who delivered at the hospital and had made one or more visits to the prenatal clinic, seven had stillbirths. Of the 276 who delivered and had no prenatal care, 11 had stillbirths.

Evaluation of Findings

Our findings would indicate that medical and hospital resources in Minneapolis are adequate for those who can afford and are motivated to use them. Prematurity, maternal, infant and perinatal mortality rates in the City compare very favorably with State and/or National rates. These favorable rates, however, do not apply evenly to all parts of the City.

We find that generally the census tracts with low socioeconomic conditions have a high incidence of prematurity and infant deaths, and of live births, illegitimacy and fertility. There are, however, some exceptions. Prematurity and infant deaths for instance are high in four census tracts in which the socioeconomic level is the same or higher than for the City as a whole. Another notable exception is census tract 42, which includes two public housing developments and is close to the bottom for average family income. This tract is high for live births, illegitimacy and fertility, but extremely low for infant deaths and only slightly higher than City average for prematurity. We have no explanation for this and can only speculate. Illegitimacy is high in this tract and many families are on ADC. Are mothers who are receiving public assistance for their children more apt to seek medical care for themselves and their children through welfare programs? Are the Minneapolis Health Department well-child clinics and public health nurses providing good preventive services to the infants and motivating mothers to get prenatal care?

Lack of Prenatal Care

Information on prenatal care for medically indigent patients delivered at Minneapolis General Hospital in 1962 shows that about 43 per cent of the expectant mothers had no prenatal care or made only one visit to the prenatal clinic. Seventy-one per cent of those who attended prenatal clinic made their initial visit in the last trimester. Of mothers having no prenatal care 4 per cent had fetal deaths, which is considerably higher than the 0.7 per cent of fetal deaths for mothers who made one or more visits to the prenatal clinic. These findings pose some questions:

1. Does lack of prenatal care contribute to prematurity, perinatal mortality and other handicapping conditions in the infant which may become financial burdens for the community?

2. Do eligibility standards for residency restrict the use of existing facilities by medically indigent patients for prenatal care?

3. Is lack of motivation on the part of the patients a primary reason for not getting adequate prenatal care?

Studies have shown that there is a relationship between lack of prenatal care and

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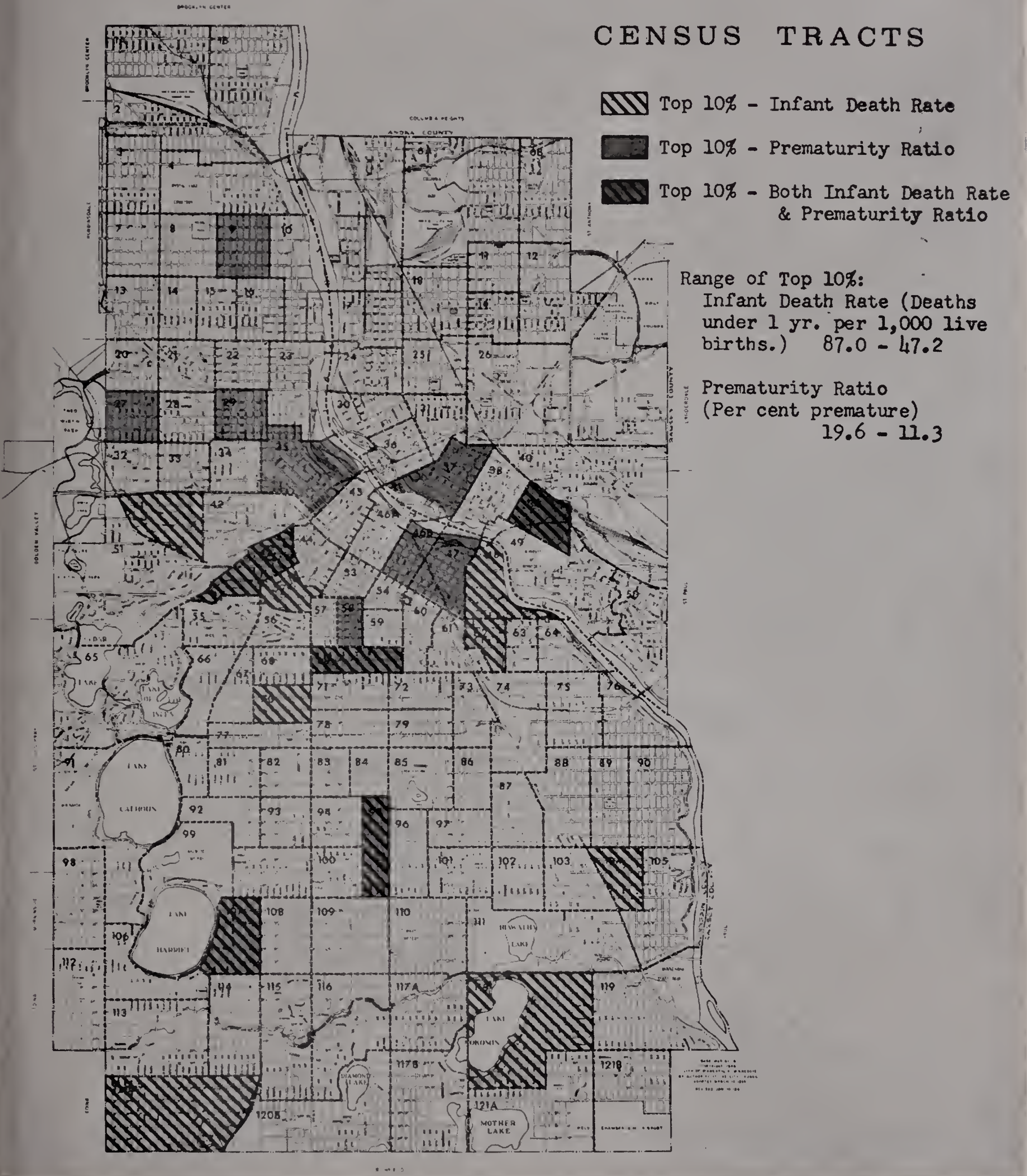
*On January 1, 1964 changed to Hennepin County General Hospital.

Map 3. Census Tracts Falling in Top Ten Per Cent For Infant Mortality and Prematurity, 1961 Minneapolis, Minnesota


CENSUS TRACTS
▨ Top 10% - Infant Death Rate
■ Top 10% - Prematurity Ratio
▩ Top 10% - Both Infant Death Rate & Prematurity Ratio
LAKE CALHOUN
LAKE HARRIET
LAKE NOKOMIS
HIAWATHA LAKE
DIAMOND LAKE
MOTHER LAKE
LAKE OF THE ISLES
ANOKA COUNTY

Range of Top 10%:
Infant Death Rate (Deaths under 1 yr. per 1,000 live births.) 87.0 - 47.2

Prematurity Ratio (Per cent premature) 19.6 - 11.3

Continued

a high incidence of prematurity and perinatal deaths.[1-3] The impact of the factor of prematurity upon neonatal mortality[4] and other perinatal casualties, including cerebral palsy,[5] has been reported. The relationship between low socioeconomic conditions and lack of prenatal care has further been stated by a WHO[6] report.

For the 276 patients who delivered at Minneapolis General Hospital in 1962 and had no prenatal care, lack of eligibility for care may have been the reason. In order to qualify for care other than emergency care, patients must meet both financial and residency requirements. For patients who made their first visit to the hospital prenatal clinic in the last trimester of pregnancy, lack of motivation for various reasons may have been the prime factor.

Obstacles to Adequate Prenatal Care[7]

1. Lack of transportation. Prenatal clinics in Minneapolis are held at General Hospital and University of Minnesota Hospitals for those eligible for care. Some private hospitals have at various times conducted prenatal clinics admitting medically indigent patients who were good teaching cases. No clinics are held in outlying neighborhoods close to the population groups needing prenatal care.

2. Problem of finding a baby sitter for other children in the family during the mother's absence.

3. Poor understanding of the need for prenatal care. Patients are probably aware of the fact that maternal deaths are rare, but lack awareness of the preventive aspects of good care to the infant. The additional advantage of mental-health support to the expectant parent through adequate prenatal care may not be recognized.

Meeting the Needs of the Indigent

Possible solutions toward meeting the needs of these medically indigent maternity patients and their infants would be: (1) set up neighborhood prenatal clinics to serve population groups that find it difficult to travel to a distant hospital clinic; (2) waive residency eligibility restrictions and admission based on arbitrary stage of gestation; (3) initiate a public health education program to motivate all expectant parents to seek early prenatal care, with special understanding of the needs and cultural differences of the economically and socially deprived; (4) intensify the public health nursing program in the low socioeconomic areas of the City to mothers and children; and (5) make provision for hospital care for high-risk maternity patients and their infants before "emergency" care is necessary.

Summary

With a few exceptions, the census tracts with low socioeconomic conditions generally had a high incidence of prematurity and infant deaths, and of live births, illegitimacy and fertility. Seventy-one per cent of expectant mothers who attended Minneapolis General Hospital Prenatal Clinic made their first visit in the last trimester of pregnancy. Of mothers who had no prenatal care, 4 per cent had fetal deaths as compared to 0.7 per cent of fetal deaths for those who had made one or more visits to the Prenatal Clinic.

Reports in literature have shown that there is a relationship between lack of prenatal care and high incidence of prematurity and perinatal deaths on the one hand; and a relationship between prematurity and neonatal mortality and other perinatal casualties on the other hand. Obstacles to adequate prenatal care have been listed.

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History of Medicine

The Tradition of Austin Flint and Alexander Skene at "Long Island"

It is a welcome privilege to prepare for MINNESOTA MEDICINE an historical introduction to the contributions of the clinical departments of the State University of New York Downstate Medical Center.

Being a descendent of Minnesota pioneers, and a Carleton graduate, as well as former Dean of the Long Island College of Medicine, and its successor in the State University, makes the task doubly enjoyable.

The selection of such outstanding figures as Austin Flint and Alexander J. C. Skene as the ones who established the great clinical tradition at the "Long Island" is inevitable, for they were of the stature to cast shadows of inspiration far into the future. Symbolic of their enduring fame is that their names are known to every student of medicine today.

Austin Flint, a graduate of Harvard Medical School in 1832, was a pupil of James Jackson, who was an enthusiastic admirer of Laennec. As a consequence, Flint became the outstanding exponent of the new approach to physical diagnosis, popularizing the use of the stethoscope, and gave his name to a previously undefined heart murmur. Samuel Gross of Philadelphia said of him, "I know of no one who is so well entitled as Austin Flint, Sr., to be regarded as the American Laennec." At Buffalo, Long Island, New York University, and New Orleans he was the great clinical teacher of his day.

He loved to work with medical students directly at the bedside and in the clinics.

At one of his characteristically scholarly lectures delivered at the beginning of his professorship at the Long Island College Hospital in September, 1860, his subject was the anemias. In discussing cases of Addisonian "idiopathic* anemia," he referred to the work of a previous investigator, a Dr. Handfield Jones, who had discovered by microscopic examination of stomachs of patients coming to autopsy that 75 out of 100 cases revealed more or less atrophy of the tubuli. Dr. Flint, in commenting on the importance of the gastric glands, could "see how fatal anemia must follow an amount of degenerative disease, reducing the amount of gastric juice so far that the assimilation of food is rendered wholly inadequate to the wants of the body." He went on to say, "I shall be ready to claim the merit of this idea when the difficult and laborious researches of someone have shown it to be correct."[1]

It was some 70 years before the "difficult and laborious researches" predicted by Austin Flint found the answer to the riddle.

Dr. William B. Castle, Francis Weld Peabody Faculty Professor of Medicine at Harvard, gave the answers in his reports, "Observations on the Etiology Relationships of Achylia Gastrica to Pernicious Anemia," in 1929, and "The Nature of Extrinsic Factor" in 1932. It was as Flint had predicted; the answer was in the gastric mucosa!

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*See Test Your Word Score Page 1639.

Continued

Alexander Johnson Chalmers Skene, after earlier studies in medicine at Toronto and Michigan, received his M.D. at Long Island College Hospital in 1863, just ten years after his idol, James Marion Sims, the creator of gynecology as a specialty, had arrived to begin his career in New York.

Skene, however, fell immediately under the influence of Austin Flint, Sr., his Professor of the Practice of Medicine and Pathology. Inevitably, his exposure to so brilliant and inspiring a teacher had a profound influence in shaping his life's work. Later it was recorded that "to no part of his professional life was he more fond of looking back than to that which he spent as an assistant to Austin Flint, Sr.," . . . from 1866 to 1867 . . . "he was proud of the skill which he then acquired in the diagnosis of cardiac and pulmonary diseases, and attributed much of his subsequent success in the treatment of his patients to his ability to recognize the existence of disordered conditions, other than those of the sexual organs, and to his appreciation of these conditions. Too often nowadays the specialist emerges fullgrown from the medical college, lacking oftentimes any general experience whatever in hospital or private practice. . . ."[2] How true today in 1965!

Skene's range of interests was broadened by his love of art, through which he became a fine amateur sculptor. A bust of J. Marion Sims, which he executed, is a treasured possession of the Medical Society of the County of Kings. He felt that this experience in sculpture was fine training for the eye and hand which could augment the skill of the surgeon.

Beginning as Assistant Professor of Obstetrics and Diseases of Women at the Long Island College Hospital in 1866, by 1870 he was Professor of Gynecology, then Dean of the Faculty, and President of the College until the end of his distinguished career.

Skene's literary contributions include associate editorships of such journals as the Archives of Medicine and the New York Gynecological and Obstetrical Journal; authorship of six books and 96 medical papers and published addresses. Since his heavy commitments to the demands of his teaching and practice filled his days, his writing was all done in the morning before breakfast!

His mechanical ingenuity caused him to devise numerous surgical instruments, the patterns of which are generally used today, without recognition of Skene's part in the invention of them. His well-known observation on the urethral glands in 1880, until that time the seat of intractable trouble, has made his name known today to every student of medicine.

One of Skene's many disciples was a kindred spirit, interested both in gynecology and the arts, Robert Latou Dickinson.

One day in the early 1880s, toward the end of a surgical clinic, Skene observed a student in the front row of the amphitheatre busily coloring a sketch he had made of the operative procedure just completed. Skene was so impressed with the artistry and fidelity of the picture that he engaged the student on the spot to illustrate his forthcoming text on gynecology!*

The student was **Robert Latou Dickinson**, whose art was so unique that it is worthy of a brief account. At the age of 10, in 1871, when he and his father were paddling a homemade canoe in the Adirondacks, he impulsively decided to dive into the river. What happened in Dickinson's own words was, "Just then a little eddy swung the canoe right under me. The stem was of galvanized iron with the top bent sharply so that the point was as keen as a knife. That's what I hit."

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*A. J. C. Skene, Diseases of Women, D. Appleton & Co., New York (1888 and 1892).

As Dr. Dickinson later told me the rest of the story, he partially eviscerated himself through an eight-inch tear in his abdominal wall, and swam ashore holding his intestines back in one hand! Inasmuch as the village doctor was too crippled with arthritis to grasp a needle holder, the local cobbler placed the sutures of waxed thread under the doctor's guidance. After weeks of drainage and the escape of some sand and pebbles, the boy recovered! That experience led him into medicine!

During his convalescence his father took him to Europe, where he had his first art lessons with pencil and brush in Paris. Upon his return he entered the Long Island College Hospital where he was inspired by Skene and thereafter maintained a lifelong passion of dual devotion to gynecology and art (both sketching and sculpture). He was a pioneer in family planning and control of conception, long before the scare term "population explosion" had been coined.

In the 1920s, Dickinson made a tour of hospitals in the interior of China, Audubon-style sketching as he went. On his return, just before I went to China, he answered my inquiry of how to keep up medically in an isolated station as follows: "Select an unsolved problem each year, record your observations exactly and systematically, read everything published about it, and write up your conclusions for publication. If you do, you won't 'go to seed' professionally."

Dr. Edward C. Rosenow, Jr., Executive Director of the American College of Physicians, was then serving as an English teacher with Carleton-In-China, in Fenchow, Shansi, but with a strong medical interest, inspired by his Mayo Clinic father. Following the Dickinson formula, he had the enterprise to determine the blood groupings of 1000 local Chinese, and published his first medical article with me in the Chinese Medical Journal, as to the biochemical index. As an important by-product of that research, a 'walking blood bank' was established, and the first transfusions in China were given in that area.

The tradition of fine clinical teaching at the bedside, in the clinic, and in the amphitheatre, nurtured throughout the earlier years at Long Island College by such stars in the academic firmament as Flint, Skene, Dickinson, and many others, has been continued into more recent years by such figures as John Osborn Polak, Alfred Beck, Charles Gordon, and Louis Hellman — worthy followers of Skene!

Emil Goetsch, a disciple of William Halsted at Hopkins and of Harvey Cushing at the Peter Bent Brigham, became the master surgeon in dealing with thyroid conditions and the preceptor of a long line of finely-trained surgeons in his pioneer residency system, the third in the United States. The eminent neurosurgeon, E. Jefferson Browder, one of that galaxy of residents, and also a preceptee of Harvey Cushing, followed Dr. Goetsch. His successor, **Clarence Dennis,** is carrying on in the same tradition as Professor-in-Charge of a great system of surgical services, including the University Hospital, Kings County Hospital, and a group of affiliated institutions.

Other figures sustained the ideals of research and teaching, such as

Continued

Dr. George M. Sternberg, Director of the first privately endowed bacteriology laboratory in the United States; The Hoagland Laboratory of Long Island College; Dr. Jean Redmond Oliver, renowned figure in renal pathology; and the revered Dr. Frank L. Babbott, Jr., President of the College from 1931 to 1941. Dr. Babbott, himself a pediatric specialist highly trained at Yale and Johns Hopkins, was instrumental in bringing in Dr. Charles Weymuller as professor-in-charge to be followed in turn by full-time chairmen, first Dr. Richard Day and then the current chairman, Dr. Jonathan T. Lanman. Drs. Luther Warren and Tasker Howard, Professors of Medicine, were followed by the brilliant Dr. William Dock, who might be styled a present-day Austin Flint. Dr. Dock, the first full-time Professor of Medicine at Long Island College of Medicine, was succeeded by Dr. Perrin H. Long and then by the present Chief of the Department, Dr. Ludwig W. Eichna.

All these and many others played essential roles in the great transition, when the Long Island College of Medicine became the nucleus in the Downstate Medical Center of the State University of New York in 1950, which now, with tremendously strengthened and enhanced faculty, facilities, teaching, research, and patient care, rounds out 105 years of medical history.

Under the leadership of Dr. Robert A. Moore, present President and Dean of the State University Medical Center for New York City, there has been rapid growth over the past decade. To the new Medical Science Building, constructed before his arrival, there has been added a new University Teaching and Research Hospital, with outpatient clinic and residences for the student body. Also to the 2800-bed university-controlled services of Kings County Hospital there has been added an impressive array of affiliated hospitals, both private and public, under full-time leadership, which have been brought under the Center's teaching and research direction, providing immense resources for internship and residency training, and a vast program of postgraduate education for physicians and other health personnel. Other developments are a collegiate nursing school and a consolidated medical library center in cooperation with the Medical Society of the County of Kings, creating one of the great resources of medical literary reference in the country.

The papers to follow from the Downstate Medical Center's clinical services reveal the extent to which the tradition set by Austin Flint and Alexander Skene and their followers continues to live!

Jean Alonzo Curran, M.D., L.L.D.*
Brooklyn, New York

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*Professor of the History of Medicine, Emeritus, State University of New York Downstate Medical Center.

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Drive Safely

A driver who has a few quick ones may have a few close ones, too.

Wall Street Journal

Medical Economics

A Brief Explanation . . .

Social Security for Physicians

If you are a self-employed doctor of medicine you are now covered by Social Security retroactive to January 1, 1965. Under the provisions of the Social Security Act of 1965, the self-employment earnings from your medical practice are subject to tax and you and your family are eligible for future social security benefits.

For the year 1965, earnings totalling $4800 will be subject to tax and the amount which you will be required to pay on or before April 15, 1966, will be $259.20. In 1966, the amount of taxable income will increase to $6600 and the tax payable will be $405.90.

It is important to note that these amounts do not include taxes which have previously been withheld from salaries and other compensations ordinarily subject to Employees Social Security tax. Withholding coverage and liability for taxes for interns and residents will not begin until January, 1966.

Physicians self-employment social security tax rates are scheduled for a progressive hike from now until 1987 as follows:

Year	Combined Tax Rate Per Cent	Maximum Earnings Subject to Tax	Maximum Tax
1965	5.4	$4,800	$259.20
1966	6.15	6,600	405.90
1967 and 1968	6.4	6,600	422.40
1969-1972	7.1	6,600	468.60
1973-1975	7.55	6,600	498.30
1976-1979	7.6	6,600	501.60
1980-1986	7.7	6,600	508.20
1987 and after	7.8	6,600	514.80

Physician Benefits are Varied

For You

Old-Age Insurance Benefits — payable when you reach age 65 (reduced benefits are payable as early as age 62), for months in which you are retired or do little or no work. Benefits are payable beginning with the month you reach age 72 even if you do not retire. Disability Insurance Benefits — payable if you become disabled before age 65.

Benefits begin for the 7th month of your disability.

For Your Family

When you are entitled to old-age or disability insurance benefits:

Wife's Benefits — to your wife at age 65 (reduced benefits are payable as early as age 62). Benefits are payable to divorced wives under certain circumstances.

Mother's Benefits — to your wife under age 62 if she has in her care an unmarried child under 18 entitled to benefits based on your earnings, or a child entitled to childhood disability benefits because of your earnings.

Child's Benefits — for your unmarried children under age 18; the payments can continue until age 22 if the child is attending school full time.

Childhood Disability Benefits — for your child over 18 if the child became disabled before reaching age 18 and has been disabled ever since.

In the Event of Your Death

Widow's Benefits — to your widow at age 62 (reduced benefits are payable as early as age 60). Benefits are also payable to surviving divorced wives under certain circumstances.

Mother's Benefits — payable to your widow under age 62 if she has in her care your child under 18 who is entitled to benefits, or your child 18 or over who is entitled to childhood disability benefits.

Child's Benefits — for your unmarried children under age 18; the payments can

Continued

continue from age 18 to age 22 if the child is attending school full time.

Childhood Disability Benefits — for your child if the child became disabled before reaching age 18 and has been disabled ever since.

Dependent Parent's Benefits — to your dependent mother or father (or both) from age 62 on, provided you were contributing one-half of your parent's support at the time of your death.

Lump-Sum Payment — in addition to any monthly benefits, a lump-sum death benefit, which may be from $132 to $255, is payable at your death.

Health Insurance at Age 65

The Health Insurance Program for the aged has two parts:

Hospital Insurance — to help pay the costs of hospital care and certain other medical services.

Medical Insurance — to help pay the costs of physicians' services and certain other medical services not covered by hospital insurance.

Both programs start July 1, 1966.

Everyone 65 or older who is eligible for cash social security benefits (including the wife of an insured person) is also eligible for protection under the hospital insurance plan.

Nearly everyone 65 or over is eligible to enroll for medical insurance. Those who enroll will pay a premium (initially $3 monthly) for the protection, and the Federal Government will pay an equal amount.

Credits for Benefits

If you are a self-employed physician, you get four quarters of credit for each year in which your net earnings from self-employment are $400 or more.

If you are an employee, you get one quarter of credit for each calendar quarter in which you are paid wages of $50 or more.

To be insured for disability benefits — you need credit for at least 5 years of work in the 10-year period ending when you become disabled.

To be insured for retirement and survivors benefits — in general, the amount of work you need depends on the year you reach age 65 (62 for women) or on the year of your death if you die before that age.

To determine the amount of work required to qualify for retirement and survivor's benefits consult the following table prepared by the Social Security Administration.

If you reach age 65 (62 for women) or die in —	You will not need credit for more than this much work —
1957 or earlier	1½ years
1958	1¾
1959	2
1960	2¼
1961	2½
1962	2¾
1963	3
1964	3¼
1965	3½
1966	3¾
1967	4
1968	4¼
1969	4½
1970	4¾
1971	5
1975	6
1979	7
1983	8
1987	9
1991 (or later)	10

No one needs credit for more than 10 years of work to be insured for retirement or survivors benefits. Survivors benefits may be payable to your children and their mother if you have social security credit for 1½ years' work out of the 3 years before your death.

Credits Allowed for Previous Work

If you have at sometime done work that was covered by Social Security you may already have Social Security for some work. Also, if you were in the military service of the United States between September 15, 1940, and December 31, 1956, you may get social security credit for your active duty (unless it is counted toward certain other Federal benefits). Military service after 1956 is covered by the law in the same way as other kinds of employment.

Amount of Benefits

The benefit amount is based upon your average earnings under Social Security. Thus being insured merely means you are eligible. It does not determine the amount of benefits payable to you or your family. The benefit amount depends on your average earnings under Social Security.

The following table gives examples of retirement benefits. Additional benefits payable to dependents are not included.

Complete Retirement Unnecessary

You don't have to retire completely to get benefits. But if you expect to work while getting benefits, it is important to know how your earnings may affect your social security payments, advises the Social Security Administration. While under age 72, your total earnings and the number of months you work are the two things which determine how much in benefits can be paid to you.

Total Earnings — if you earn no more than $1,500 for a year after 1965, you will get benefits for all months for which you are otherwise entitled.

If you work throughout the year and earn more than $1,500, $1 in benefits will be withheld for each $2 you earn between $1,500 and $2,700. For every $1 that you earn over $2,700, $1 in benefits will be withheld.

Contact your local Social Security office if you have questions about Social Security, if you need a Social Security account number card, or if you wish to apply for benefits.

Born In		Retire In					
Man	Woman	1966	1967	1968	1969	1970	1971
1892 or earlier	1895 or earlier	$87.80	$112.40	$138.00	$161.00	$168.00	$168.00
1897	1900	——	101.70	122.00	143.00	163.00	168.00
1899	1902	——	——	102.80	118.80	133.80	149.00
1901	1904	——	——	91.00	103.80	116.70	128.40
1903	1906	——	——	——	93.10	103.80	114.50
1905	1908	——	——	——	——	95.30	104.90

Fatty Tumours

The steatoma is an abnormal growth of fat, which varies according to the nature of its site. It is of a uniform colour, yielding to the touch; at first it is small, but in time it enlarges. Most of them have their greatest circumference at the base; rarely they are found with a narrow base and widening towards the summit.

The fatty tumour differs from the strumous in being softer to the touch; it differs from the atheroma or the meliceride in being solid and not pitting on digital pressure; it also is cured by operation.

In operating, the incision is made right across the summit of the tumour, and is either simple or myrtle-leaf shaped according to the tumour. The capsule is now boldly cut away, for in these cases we do not fear sinus-formation in connection with the sac, as in melicere tumours or atheromas, since here the fat does not fall out when cut into. And there is another thing to bear in mind, as has been pointed out regarding strumous glands: if the steatoma is merely attached, one secures it by stripping it at the sides and below and shelling it out, now with the fingers and now with the handle of the knife; but, if it be closely adherent, then it must be dissected out. Then, after removal, the lips are stitched up, with a view to union; otherwise the bottom of the wound may be drained, and treatment by suppuration promoted.

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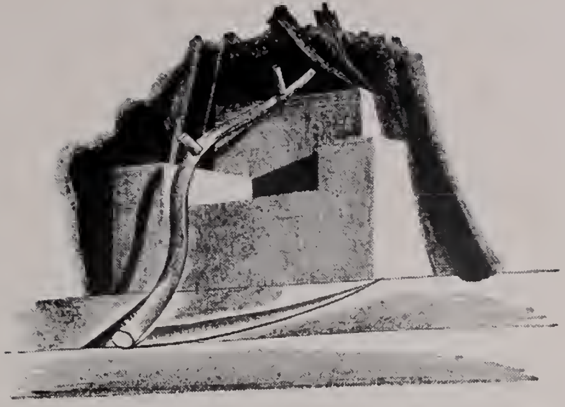

In Memoriam

Death is the liberator of him whom freedom cannot release; the physician of him whom medicine cannot cure; the comforter of him whom time cannot console.
— Colton

Death cannot come untimely to him who is fit to die. — The less of this cold world the more of heaven, the briefer life, the earlier immortality. — Milman.

JULIUS J. HEIMARK, M.D.

Dr. Julius J. Heimark, 77, Fairmont physician for thirty years prior to his retirement five years ago, died September 24th, in Phoenix, Arizona, following a stroke. Dr. Heimark was one of the founders of the Fairmont Clinic and Hospital, now the Fairmont Community Hospital.

He was born in Clarkfield, Minnesota, and graduated from the University of Minnesota Medical School. During his lifetime, Dr. Heimark belonged to many medical and civic organizations.

He is survived by his wife, a daughter, and two sons, one of whom is Dr. John Heimark of Mankato.

JACK R. PIERCE, M.D.

Dr. Jack R. Pierce, 46, former Virginia physician, died July 4th, at Buffalo, New York General Hospital. He was born in Arcade, New York, and graduated from the University of Buffalo Medical School. He practiced in Virginia for seven years before moving to Bradford, Pennsylvania.

He is survived by his wife and six children.

DANIEL E. GREENE, M.D.

Dr. Daniel Edward Greene, 50, Warren physician, died September 2nd. He was born in Pharr, Texas, and received his medical degree at the University of Omaha.

During his youth, Dr. Greene excelled in many sports and at one time was offered a career in professional baseball, however, he chose the medical profession. He was a member of many civic groups and a member of the Red River Valley Medical Society, Minnesota State Medical Association, and American Medical Association.

He is survived by his wife, two daughters and a son.

LEONARD T. CARLSON, M.D.

Dr. Leonard T. Carlson, 61, Minneapolis physician, died October 19. He was on the staffs of North Memorial and Glenwood Hills Hospitals, and medical examiner for the Selective Service Board since 1941.

He was born in Minneapolis and received medical degree at the University of Minnesota. He was a member of the Hennepin County Medical Society, the Minnesota Medical Association, American Medical Association, and the American Academy of General Practice.

He is survived by his wife, a son and a daughter.

L. HAYNES FOWLER, M.D.

Dr. L. Haynes Fowler, 69, formerly of Minneapolis, died October 13, in Newport Beach, California. He was born in Binghamton, New York, and received his medical degree at the University of Minnesota.

Dr. Fowler was a Minneapolis surgeon for thirty-five years before his retirement. He was associated with University Hospital and the Northwestern Hospital, and a fellow of the American College of Surgeons. He was a member of the Hennepin County Medical Society, Minnesota State Medical Association, and the American Medical Association.

He is survived by his wife.

ANNOUNCING

THE TWENTY-NINTH ANNUAL MEETING
of
THE NEW ORLEANS GRADUATE MEDICAL SCHOOL

Conference Headquarters — Roosevelt Hotel

March 7, 8, 9, 10, 1966

GUEST SPEAKERS

Robert J. Rowe, M.D., Dallas, Tex.—*Colon and Rectal Surgery*
Walter C. Lobitz, Jr., M.D., Portland, Ore.—*Dermatology*
Bernard J. Haverback, M.D., Los Angeles, Calif.—*Gastroenterology*
Joseph J. Rupp, M.D., Philadelphia, Pa.—*General Practice*
Roy T. Parker, M.D., Durham, N. C.—*Gynecology*
Stefan S. Fajans, M.D., Ann Arbor, Mich.—*Internal Medicine*
John S. LaDue, M.D., New York, N. Y.—*Internal Medicine*
Joseph M. Foley, M.D., Cleveland, Ohio—*Neurology*
Duncan E. Reid, M.D., Boston, Mass.—*Obstetrics*
H. Saul Sugar, M.D., Detroit, Mich.—*Ophthalmology*
S. Benjamin Fowler, M.D., Nashville, Tenn.—*Orthopedic Surgery*
Walter P. Work, M.D., Ann Arbor, Mich.—*Otorhinolaryngology*
William O. Russell, M.D., Houston, Tex.—*Pathology*
William A. Silverman, M.D., New York, N. Y.—*Pediatrics*
C. Allen Good, M.D., Rochester, Minn.—*Radiology*
Louis M. Rousselot, M.D., New York, N. Y.—*Surgery*
Jerome A. Urban, M.D., New York, N. Y.—*Surgery*
Donald R. Smith, M.D., San Francisco, Calif.—*Urology*

Additional Speaker to be Announced

Lectures, symposia, clinicopathologic conferences, round-table luncheons, medical motion pictures, technical exhibits and entertainment for visiting wives. (All-inclusive registration fee—$25.00).

This program is acceptable for twenty-nine (29) accredited hours by the American Academy of General Practice.

The Clinical Tour AROUND THE WORLD visiting Hawaii, Tokyo, Nikko, Kyoto, Nara, Hong Kong, Bangkok, New Delhi, Agra, Jaipur, and Cairo. Leaving March 12 via air and returning April 12, 1966.

For information concerning the Assembly meeting and tour write Secretary, The New Orleans Graduate Medical Assembly, Room 1528, 1430 Tulane Avenue, New Orleans, Louisiana 70112.

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Meetings and Announcements

Dishonesty will stare honesty out of countenance any day in the week, if there is anything to be got by it. — Dickens

DECEMBER

Minnesota Obstetrical & Gynecological Society, December 4, 9:00 a.m., Miller Hospital, St. Paul.

American College of Cardiology & The Minnesota Heart Association, December 4, symposium at Sheraton-Ritz Hotel, Minneapolis, on the subject: "Catecholamines & Adrenergic Blocking Agents."

Minnesota Academy of Medicine, December 8, 6:30 p.m., Town & Country Club, St. Paul.

St. Louis County Medical Society, December 9, Executive Committee, 6:00 p.m., St. Luke's Hospital, Duluth.

St. Louis County Medical Society, December 18, Annual Dinner-Dance, 7:30 p.m., Kitchi-Gammi Club, Duluth.

University of Colorado School of Medicine Symposium on Menstrual Mechanisms, December 6-7, Denver, Colorado. Contact: University at 4200 East 9th Avenue, Denver.

American College of Physicians will hold a regional meeting at the Pioneer International Hotel, Tucson, Arizona, December 4th. Contact: Charles Stephens, M.D.; 2430 Sixth Street, Tucson, Arizona.

JANUARY

Hennepin County Medical Society, January 3, 6:00 p.m., Pick-Nicollet Hotel, Minneapolis.

Hennepin County Psychiatric Society, January 3, Held in connection with Hennepin County Medical Society.

Zumbro Valley Medical Society, January 5, 8:00 p.m., Mann Hall, Rochester, new officers take positions.

Minnesota Academy of General Practice & Hennepin County Medical Society, January 10, Lederle Symposium, all day, Radisson Hotel, Minneapolis.

Minnesota Academy of Medicine, January 12, 6:30 p.m., Town & Country Club, St. Paul.

St. Louis County Medical Society, January 13, Executive Committee, 6:00 p.m., St. Mary's Hospital, Duluth. Annual business meeting, 8:00 p.m.

Twin City Urological Society, January 21, 6:00 p.m., Town & Country Club, St. Paul.

Ramsey County Medical Society, January 31, 8:00 p.m., 1500 Lowry Medical Arts Building, St. Paul.

American College of Surgeons Sectional Meeting, Bal Harbour, Florida, January 13-15, Americana Hotel. Contact: American College of Surgeons, 55 East Erie Street, Chicago.

30th Annual Session of the International Medical Assembly of Southwest Texas, January 24-26, Granada Hotel, San Antonio Texas. Contact: Bernard Fein, 202 W. French Place, San Antonio.

ANNOUNCEMENTS

Conference on Pediatric and Adolescent Gynecology will be held March 24, through March 26, 1966, at the Waldorf-Astoria in New York City, under the auspices of the New York Academy of Sciences. Contact: Warren Lang, M.D.; Jefferson Medical College of Philadelphia, 1025 Walnut Street, Philadelphia.

* * *

Dr. Birger Strandell, a member of the faculty of the Caroline Institute, Stockholm, and editor of ACTA MEDICA SCANDINAVICA, will lecture on "Linnaeus" at Rochester, May 10, 1966. The lecture, sponsored by the Mayo Foundation chapter of Sigma XI, will be held a day before the opening of the annual meeting of the American Association for the History of Medicine. Contact: Thomas E. Keys, 200 First Street Southwest, Rochester, Minnesota.

* * *

Minnesota Heart Association and American College of Cardiology Symposium, December 4 (one day) at the Sheraton-Ritz Hotel in Minneapolis. Subject will be: "Adrenergic Blocking Agents with Special Reference to Hypertension and the Catecholamines." Contact: Executive Secretary of American College of Cardiology, 9650 Rockville Pike, Washington, D.C. or the Minnesota Heart Association Office in St. Paul.

* * *

The twenty-ninth annual meeting of The New Orleans Graduate Medical Assembly will be held March 7, 8, 9 and 10, 1966, headquarters at The Roosevelt Hotel.

Nineteen outstanding guest speakers will participate and their presentations will be of interest to both specialists and general practitioners. This program is acceptable for twenty-nine (29) accredited hours by the American Academy of General Practice, Write Secretary, New Orleans Graduate Medical Assembly, 1430 Tulane Avenue, Room 1528, New Orleans, Louisiana 70112.

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The Blue Shield

Blue Shield of Minnesota, the state's largest medical-surgical plan, has taken another step for its future growth.

Since 1961, it has already grown about 36 per cent financially.

In 1965, if present trends continue, Blue Shield will have a $2 million growth year — double that of 1964.

In July, to continue its progress, Blue Shield moved into its new state headquarters at 2344 Nicollet Avenue in Minneapolis — an office building of more than double the office space Blue Shield had at 2218 University Avenue.

Paradoxically, Blue Shield, in its colorful history, is both an "old timer" and a young company.

Now 18 years old, it is one of the younger business organizations in the state. Yet, when it was founded in 1947 by doctors of medicine in Minnesota, it was the first medical-surgical organization in the state. It is, despite its few years, the pioneer health care plan of its type in Minnesota.

In 1947 the organization had no competition and grew rapidly. Today, in the face of competition from several hundred insurance organizations within the state, and several thousand insurance organizations throughout the U. S., it has had a growth rate of $1 million per year for the past four years. In 1961, Blue Shield had total revenues of $10.8 million. At the end of 1964, revenues reached $14.7 million.

By the end of this year, with an anticipated $2 million growth, Blue Shield will be nearly a $17 million organization.

A significant portion of Blue Shield's growth came from the improvement of coverage for existing subscribers.

Under the direction of the Blue Shield Board of Directors, the organization since 1961 has produced better medical-surgical plans, new hospital coverage plans, major medical coverage as well as more inclusive senior citizen coverage.

In 1961, Blue Shield entered the hospital coverage field by developing a hospital "rider" to its medical-surgical contract. The hospital coverage plan has a wide range of coverages to meet the various cost levels throughout the state. Daily room allowance plans can be purchased from $10 to $25 a day, with coverages from 30 to 720 days in group contracts.

The following year, and on an experimental basis, Blue Shield introduced its M-Series plan. This plan, which has since become available to the general public, is based on a new medically developed "relative value index."

It offers "Paid-In-Full" features to people whose incomes are up to $7,500 a year.

Also, Blue Shield developed a $20,000 Major Medical Contract. Sold only with the basic Blue Shield medical-surgical coverage, Major Medical pays up to $20,000 after a $100 deductible and on an 80/20 co-insurance basis. Its cost today ranges up to 60¢ a month for an individual and up to $1.20 for a full family. It is sold only to groups of ten or more people.

Blue Shield, which had a medical-surgical senior citizen program since 1959, offered a new and wider health care program in 1964 to people over age 65. The plan offered not only medical-surgical care but 90 days of hospitalization for each illness each year, plus 60 days of nursing home care.

Late last year, Blue Shield began supplementing its direct sales force with an "agency broker" system outside the Twin Cities to supplement its regular sales force. Now nearly 40 agents in rural Minnesota are handling Blue Shield for local customers.

Also in 1964, in one of the first acts of its kind in Minnesota, the Saint Louis County Board approved a plan in which Blue Shield would administer a program of medical care for welfare patients. The program is planned to begin late in 1965.

The organization has also been active in an intensive management development program, which has resulted in some dramatic changes, including increased sophistication of operation and substantial corporate growth. This effort was enhanced by the recruiting of a few top executives from outside the company. From Minneapolis General Hospital, Blue Shield gained its new controller and from an insurance company in Wisconsin, came its new marketing director. Blue Shield also hired new actuaries as well as new advertising and public relations consultants.

For the past several years, Blue Shield has been undergoing a reorganization toward more of a marketing rather than a "product" oriented company.

The increased service has brought to Blue Shield new departments and increased personnel. In 1960, Blue Shield had 38 employees. Today, the plan has nearly 200 people, most of which are at the state headquarters in Minneapolis, The balance are representatives throughout the state or people attached to Blue Shield's Duluth office.

Thus, Blue Shield, the first organization in the medical-surgical field in Minnesota, is undergoing a new period of growth.

When you sow wild oats, you always get a bumper crop. — Herbert Prochnow

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Physician's Diary

Nations, like individuals, live or die, but civilization cannot perish. — Mazzini

Dr. R. O. Sather of Crookston has been appointed medical director of the Sunnyrest Sanatorium.

* * *

Dr. Edward W. Ciriacy, Ely, was chosen president-elect of the Minnesota Academy of General Practice at the annual business meeting held in September, and **Dr. Herb L. Huffington** of Waterville assumed the presidency of the Academy at this same meeting. **Dr. C. A. Anderson** of Hector was sworn in as secretary-treasurer.

* * *

Dr. Howard M. Wikoff of Crookston was elected chief-of-staff of the Bethesda Hospital in Crookston. **Dr. O. K. Behr** was elected vice president, and **Dr. A. R. Reff** elected secretary.

* * *

Dr. James M. Thomson is leaving Austin after twenty-five years of practice in the area. Dr. Thomson is a certified specialist in obstetrics and gynecology.

* * *

Dr. J. Lee Sander of Cambridge has passed the written and oral examinations for the American Board of Surgery and is now a diplomate in the board.

* * *

Dr. Randolph M. McCloy, a fellow in gastroenterology, was elected president of the Association of Fellows of the Mayo Graduate School of Medicine at an annual meeting of the organization. Other new officers are: **Dr. David L. Ahmann**, vice president; **Dr. Drake D. Duane**, secretary and **Dr. Betty L. Mundy**, treasurer.

* * *

Dr. R. C. Magnuson and his family are touring the Middle East. After a tour of the Holy Land, they will be spending three months at the Baptist Mission Hospital in Gendeberet, Ethiopia, with **Dr. Tom P. Coleman. Dr. Magnuson** is associated with the Cambridge Clinic in Cambridge.

* * *

River's Edge Medical Clinic in Farmington received an honorable mention at the ninth annual honor awards program of the Minnesota Society of Architects.

Dr. Reuben Berman of Minneapolis, has been elected president of the Minnesota Heart Association. Other officers named were: **Dr. Ivan D. Frantz, Jr.** of St. Paul, president-elect, and **Dr. John L. Juergen**, Rochester, secretary.

* * *

Dr. Alvin Schultz has been appointed the director of the department of medicine at Hennepin County General Hospital. He will take over his duties on November 1st. Dr. Schultz was chief of medical research and education at Mount Sinai Hospital in Minneapolis.

* * *

Dr. Richard J. Wett of Minneapolis was recently elected a fellow of the American Society of Anesthesiologists, and **Dr. W. Sawyer Eisenstadt** of Minneapolis was recently elected to the Board of Regents of the American College of Allergists.

* * *

Dr. George C. Flora of the Department of Psychiatry and Neurology at the University of Minnesota was one of the recipients of the "distinguished teaching awards" presented by the Minnesota Medical Foundation, and **Dr. Sidney K. Shapiro** was elevated to Clinical Professor of Psychiatry and Neurology at the University of Minnesota College of Medical Sciences.

* * *

NEW LOCATIONS: **Dr. Quentin Knauer** will join Doctors Jose and Alayne Aruguete in Sandstone . . . **Dr. John W. Foderick** will associate with **Dr. Herman J. Just** in Hastings . . . **Dr. John T. Goswitz** will join the Mankato Clinic staff . . . **Dr. Gerald W. Ireland** will leave the Itasca Clinic to specialize in urology at the University of Minnesota . . . **Dr. Ronald Ohmann** of Mound has joined the staff at the Glencoe Clinic . . . **Dr. Robert Nelson** has left Benson for Wake Island where he will be employed by the Federal Aviation Agency . . . **Dr. Jurgen Moller** of Farmington has taken a residency in anesthesia at the University of Minnesota . . . **Dr. Robert G. Carlson** of Willmar has entered the study of heart and chest surgery at the University of Minnesota . . . **Dr. Richard J. Snyder** has joined the department of obstetrics and gynecology of the Mankato Clinic.

11:47 pm 11:53 pm 12:06 am

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WANTED LOCUM TENENS. Doctor desires generalist to work for month of February 1966 in one (1) doctor clinic. Write Brainerd Clinic, Box 408, Brainerd, Minnesota.

BADLY NEEDED — G.P., Internist or Surgeon to associate with two-man G.P. partnership. Unopposed territory. New hospital, nursing home, children's home! Superb hunting, fishing, golf, pool, winter arena. Progressive town! Delmore Clinic, Roseau, Minnesota 56751.

A 13 MEMBER specialty group in the Midwest will need several men to replace and add to present staff. This has been a rewarding group for years, is now, and will be for years to come. We need 3 internists, 1 dermatologist, 1 ob-gyn, 1 pediatrician, 1 general and thoracic surgeon, 1 orthopedist, 1 ophthalmologist, 1 otorhinolaryngologist, and 1 psychiatrist. This is a very good town for a family man. Three colleges (1 a State College). Good schools and excellent recreation programs. Good hunting, fishing and water sports. Applicants should be board certified or completing requirements. Write MINNESOTA MEDICINE — 324; 496 Lowry Medical Arts Building, St. Paul 55102.

PART TIME INTERNIST OR GENERAL PRACTITIONER. Good compensation — Midway Area. Alfred F. Anderegg, M.D.; 2500 Como Avenue, St. Paul, Minnesota.

WANTED: Board Certified or eligible internist to associate with group in large, active practice in Minneapolis. Group consists of Surgeon, Obstetrician, Pediatrician and Internist maintaining downtown and suburban offices. Partnership in mind. Contact: Jesse J. Barron, M.D., 1127 Medical Arts Building, Minneapolis, Minnesota 55402, FEderal 2-8259.

WHITE BEAR LAKE, MINNESOTA. A suburban community of 35,000 and growing fast. Available several ground floor air-conditioned suites in fireproof building in central business district, free municipal parking lot at second entrance in rear. See: N. R. Dittberner, 316 Washington Avenue, White Bear Lake. Telephone: Collect anytime 429-7787.

BUSY, GROWING aggressive 3-man partnership in Northwest Wisconsin serving a trade area of 15,000 needs a well-trained recent graduate with fulfilled military obligations to associate immediately on excellent salary, with partnership in 1 year if mutually agreeable. Modern 15 room air conditioned brick clinic building is being doubled in size this year. 32 bed hospital and new 42 bed nursing home one minute from clinic. New 1500 student consolidated school. Excellent hunting, fishing and outdoor sport facilities in immediate area. Contact: MINNESOTA MEDICINE — 317; 496 Lowry Medical Arts Building, St. Paul 55102.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE — 289; 496 Lowry Medical Arts Building; St. Paul, 55102.

WANTED: Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty seven bed hospital, X ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact: A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

OFFICE SPACE now available in busy Bloomington. 713 square feet of new space in building with busy group of G.P.'s, dentist and suburban OB-GYN office. Ideal for ophthalmology, ENT or pediatrics. 8040 Penn Avenue South. 888-9211.

WANTED INTERNIST, Board qualified or certified for 22-physician mixed group of general practitioners and specialists (East Range Clinic, Virginia, Minnesota). Salary first year, then full partnership. Centrally located in area of rapidly expanding economy.

Continued

Photographic Contest

The Editors of MINNESOTA MEDICINE, in collaboration with the Doctors' Photographic Society of Minneapolis, take pleasure in announcing a monthly photographic contest. The contest is to promote an interest in photography in the medical profession. First prize each month will be publication in full color of the winning picture in MINNESOTA MEDICINE.

The following rules will govern the conduct of the contest:

1. Only doctors of medicine are eligible to submit pictures, and the picture must have been taken or composed by a physician.
2. Each contestant may submit not more than two pictures each month.
3. Only color transparencies, 35 mm. to 2¼", can be considered.
4. Each slide should be labeled with the maker's name, address, and the identifying title.
5. Slides should not be mounted on glass, but can be protected in plastic sleeves or envelopes.
6. Each entry must be accompanied by a self-addressed, stamped envelope if return of the picture is desired. Returns will be made shortly after the close of the contest each month. The winning photograph will be retained but will be returned after it has been used.
7. The deadline date for entry will be the 10th of each month and the winner of each month's contest will be announced in MINNESOTA MEDICINE in the subsequent issue. The date of publication will be three to six months in advance.
8. There will be no limitation on subject material except as indicated in item 10.
9. Model releases will be requested of winners where appropriate.
10. Judges will be selected by the editors of MINNESOTA MEDICINE and the Doctors' Photographic Society. The judges will be guided by the precepts of the Photographic Society of America, and winners will be based on appropriateness, interest, impact, and technical excellence.
11. The editors of MINNESOTA MEDICINE and the Doctors' Photographic Society cannot be responsible for entries lost or damaged, but every effeort will be made to protect submitted pictures.

Your pictures are hereby invited. Please submit pictures to:

Photo Contest Editor
MINNESOTA MEDICINE

WANTED: one or two general practitioners. Excellent clinic and hospital facilities. Rural practice established 18 years. Salary open, partnership if compatible. Lloyd H. Klefstad, M.D., Greenbush, Minnesota.

SACRED HEART, MINNESOTA, doctorless since 1961, wants general practitioner. Population 700, accredited hospital 10 miles away. Write: Rev. Robert Bardy, Phone 765-2547, Sacred Heart, Minnesota.

A THREE MAN group needs a fourth general practitioner in a fast-growing West St. Paul area. Begin with salary and join partnership with full participating advantages. Write: MINNESOTA MEDICINE — 326, 496 Lowry Medical Arts Building, St. Paul 55102.

GENERAL PRACTICE Minnetonka, 20 minutes from Minneapolis loop. Ideal location for solo start with expansion to clinic. New building. Hospital nearby. Good parking. Dentist now located in one wing. Call or write: Cliff Kommedahl, 12401 Minnetonka Blvd., Minnetonka, Phone 935-8247.

GENERAL PRACTITIONER WANTED: to associate with physician-surgeon in Owatonna, a Southern Minnesota community, 25,000 population. Clinic building three years old; with five large treatment rooms, lab.; x ray; central supply; two doctors' offices; pharmacy; and business offices. Located next door to 85 bed city hospital. Good opportunity for partnership. Contact: O. W. Roberts, M.D.; 920 South Cedar Street; Owatonna, Minnesota. Phone 451-4630.

LOCUM TENENS wanted for general practice in St. Paul from mid-February through March, 1966. Write: MINNESOTA MEDICINE — 328; 496 Lowry Medical Arts Building, St. Paul 55102.

MEDICAL ART. Drawings, charts and lettering for publication, slide lectures, movies, exhibits and television. Also three dimensional models. Al Hage — 339-1012, Minneapolis.

GENERAL PRACTITIONER AVAILABLE. Completing military June, 1966. Five years experience; married, desires group practice Rochester, Minneapolis, St. Paul or surrounding area, minimum OB and surgery. Write MINNESOTA MEDICINE — 331, 496 Lowry Medical Arts Building, St. Paul, Minnesota.

WANTED: young general practitioner to join six-man group consisting of 4 GPs, a general surgeon, and radiologist. College town of 5,500, 30 miles from Twin Cities. Also need LOCUM TENENS in general practice. Contact: Ed Jenkins, Mgr., River Falls Medical Clinic, River Falls, Wisc. Phone 425-5322.

WANTED locum tenens for month of February 1966. Can live in my home. If married, bring wife and children. Modern hospital and clinic, consultation available. Contact as soon as possible by mail or telephone: Wm. C. Heiam, M.D., Cook, Minnesota. Telephone: 666-3354 or 666-2261.

PHYSICIAN (General Medicine or Surgery) at 245 bed VA General Hospital in scenic Black Hills. Area offers excellent hunting, fishing, recreation. Requirements: Graduate approved school, citizenship, license any state, salary based on qualifications, housing available. Nondiscrimination in employment. Contact Chief of Staff, VA Center, Hot Springs, South Dakota 57747.

WANTED: Psychiatrist and general physician for full time staff positions in private psychiatric hospital currently in process of increasing range of inpatient and outpatient services. Midwest metropolitan area. Private practice opportunities after one year. Salary open according to qualifications. Attractive working conditions. Fringe benefits. Write: MINNESOTA MEDICINE — 333, 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED SOMEONE in East Side St. Paul general practice who would desire temporary locum tenens, one, two or three months. Write: MINNESOTA MEDICINE — 335, 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED: Generalist desiring fast start in too busy St. Paul practice. No covenants or contingent clauses. You move to available nearby independent office facilities as soon as you establish an adequate following of your own, or you stay as a partner if you desire. Incidentally lousy working conditions: new building, built-in Hi-fi, every third week off. If you desire to establish yourself permanently in present location. You name your own terms. Write MINNESOTA MEDICINE — 336, 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED: Immediate opening for Young GP in an established medical corporation. Three man G.P. group located in rapid-growing North Suburban Metropolitan Area. 15 minutes from loop and large educational center. New clinic. New 150-bed hospital. Salary open, fringe benefits. Fridley Medical Center, P.A., 203 Mississippi Street, Minneapolis, Minnesota 560-2950.

THE FOLLOWING LABORATORY TESTS ARE AVAILABLE TO PRACTICING PHYSICIANS: *Fluorescent Anti-nuclear Antibodies (FANA):* A broad spectrum immunological method used in the diagnosis of autoimmune diseases. *Quantitative Latex Fixation for Rheumatoid Arthritis:* The titration of rheumatoid factor (s) in the diagnosis and follow-up of rheumatoid arthritis patients. *Anti-thyroglobulin Antibodies:* Used in the diagnosis of Hashimoto's thyroiditis. *Anti-mitochondrial Antibodies:* These are present in primary biliary cirrhosis cases. The test is used to differentiate this condition from surgical obstructive jaundice cases. *Macroglobulin Precipitin test:* This test is positive in Waldenström's macroglobulinemia and other related malignant conditions. *Protein Electrophoresis* in serum, urine, and spinal fluid. Fast one-day service. Mail *2 cc serum,* nonhemolized for one or more of the above tests. For more information write or call collect: Muharrem Gökcen, M.D., Ph.D., Research Laboratories, Glenwood Hills Hospitals, Minneapolis, Minnesota 55422, Phone: 612-588-9401. Booklets are available upon request.

FOUR STAFF ADDITIONS to Southern California Group of 24 physicians. Internist with chest subspecialty, ophthalmologist, otolaryngologist, general practitioner. Partnership possibility after first year. Administrator, Gallatin Medical Group, 10720 S. Paramount Blvd., Downey, Calif.

GENERAL PRACTITIONER — to join established group in progressive city of 15,000. Excellent clinic and hospital facilities. Salary open. For details contact: Richard Lehigh, Manager, Owatonna Clinic, 134 Southview, Owatonna, Minnesota 55060.

Continued

CLASSIFIED ADVERTISING

WANTED: Young internist and pediatrician, board certified or eligible, to join 6-man group consisting of 4 GP's, a general surgeon, and a radiologist. College town of 5,500 only 30 miles from Twin Cities. Salary open with early partnership opportunity. Write or call collect: Ed Jenkins, Mgr., River Falls Medical Clinic, River Falls, Wisc., phone 425-5322.

EXCELLENT and immediate opening for one or two physicians. 17 bed fully equipped municipal hospital with lab and x-ray facilities. Also private 40 bed nursing home. Complete clinic, including equipment, available for rent. Doctor owner retiring because of ill health. No investment needed. Prosperous agricultural community. Opportunity for rewarding lifetime practice. Phone 669-4421 collect, Clarkfield, Minnesota Hospital.

PSYCHIATRIC RESIDENCIES, positions available July 1966. Fully approved, balanced didactic and clinical experiences. Five-year career program: $8,895, $10,294, $12,048, $15,368, $16,203; NIMH general practitioner stipends $12,000 annually for three years in Michigan's water winter wonderland. Paul E. Kauffman, Ph.D., Director of Resident Training, Traverse City State Hospital, Traverse City, Michigan. An equal opportunity employer.

WANTED: General practitioner able to do surgery. Present physician wanting to "semi-retire." Good community, prosperous farming. Good schools and churches. New hospital and clinic buildings. Contact: Warren Clinic, P.O. Box 107, Warren, Minnesota 56762.

WANTED: Young G.P. for rural practice partnership. No initial investment. Previous partner and well equipped for dual practice. Good hospital — 12 miles and large medical center 30 miles on four lane highway. Small town in stable farming community, resort area, hunting and fishing, good school system. Contact: A. S. Mithune, M.D., Lake Park, Minnesota.

WANTED: Associate general practice. Minneapolis. No obstetrics. Excellent hospital affiliations. Postgraduate course available University Minnesota. Superb restaurants, Tyrone Guthrie Theatre, Symphony Orchestra. Unsurpassed boating, swimming, fishing. Prefer physician with service obligation completed. $18,000 first year; partnership thereafter. Write: A. L. Walonick, M.D.; 3015 Utah Avenue South, Minneapolis 55426

RELAXED, GRACIOUS COUNTRY LIVING viewing St. Croix River. Spacious, 3-bedroom, modern home on two acres — amidst stately shade trees. Recreation room. 17 miles to St. Paul. Write: Harlan Fisher, Route 5, Stillwater, Minnesota. Telephone 436-8844.

WANTED — Internist, board certified or qualified, to associate with two board certified internists. Ten man multi-specialty group. (Lenont Peterson Clinic, Virginia, Minnesota) — Heart of the expanding taconite industry.

FOR RENT: Successful medical building. Will help doctor or group of doctors get started in proven location in Northwest Suburban Minneapolis, 36th and Noble near two hospitals. Call or write Noble Drug, 4705 36th Avenue North, Minneapolis 22. Ju 8-9449.

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benactyzine hydrochloride 1 mg.

Indications: 'Deprol' is useful in the management of depression, both acute (reactive) and chronic. It is particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination. It is also useful for management of depression and associated anxiety accompanying or related to organic illnesses.

Contraindications: Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

Precautions: *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of preexisting symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

Benactyzine hydrochloride—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

Supplied: Light-pink, scored tablets, each containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.
Before prescribing, consult package circular.

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INSOMNIA
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TRY DEPROL® meprobamate 400 mg. + benactyzine hydrochloride 1 mg.

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FOR DEPRESSION

even when complicated by anxiety, tension, insomnia, agitation or rumination.

- Acts rapidly.
- Side effects at recommended dosage infrequent, usually easily controlled.

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Description: Hygroton, brand of chlorthalidone, is an oral diuretic agent of value in the treatment of edema and hypertension. The drug is notable for its prolonged action (48-72 hours) and low toxicity. It is not a thiazide and may often be employed successfully in patients who are intolerant of other agents or become refractory to them.
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Warning: With administration of enteric-coated potassium supplements, the possibility of small bowel lesions should be kept in mind.
Precautions: Reduce dosage of concomitant antihypertensive agents by at least one-half. Discontinue if the BUN rises or liver dysfunction is aggravated. Electrolyte imbalance and potassium depletion may occur; take special care in cirrhosis or severe ischemic heart disease, and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended.
Side Effects: Agranulocytosis, constipation, dizziness, dysuria, headache, hyperglycemia, hyperuricemia, impotence, leukopenia, muscle cramps, nausea, postural hypotension, purpura, thrombocytopenia, transient myopia, urticaria, vomiting and weakness.
Average Dosage: One tablet (100 mg.) daily with breakfast.
Availability: Tablets of 100 mg. in bottles of 100 and 1000. For full details, see the complete prescribing information.

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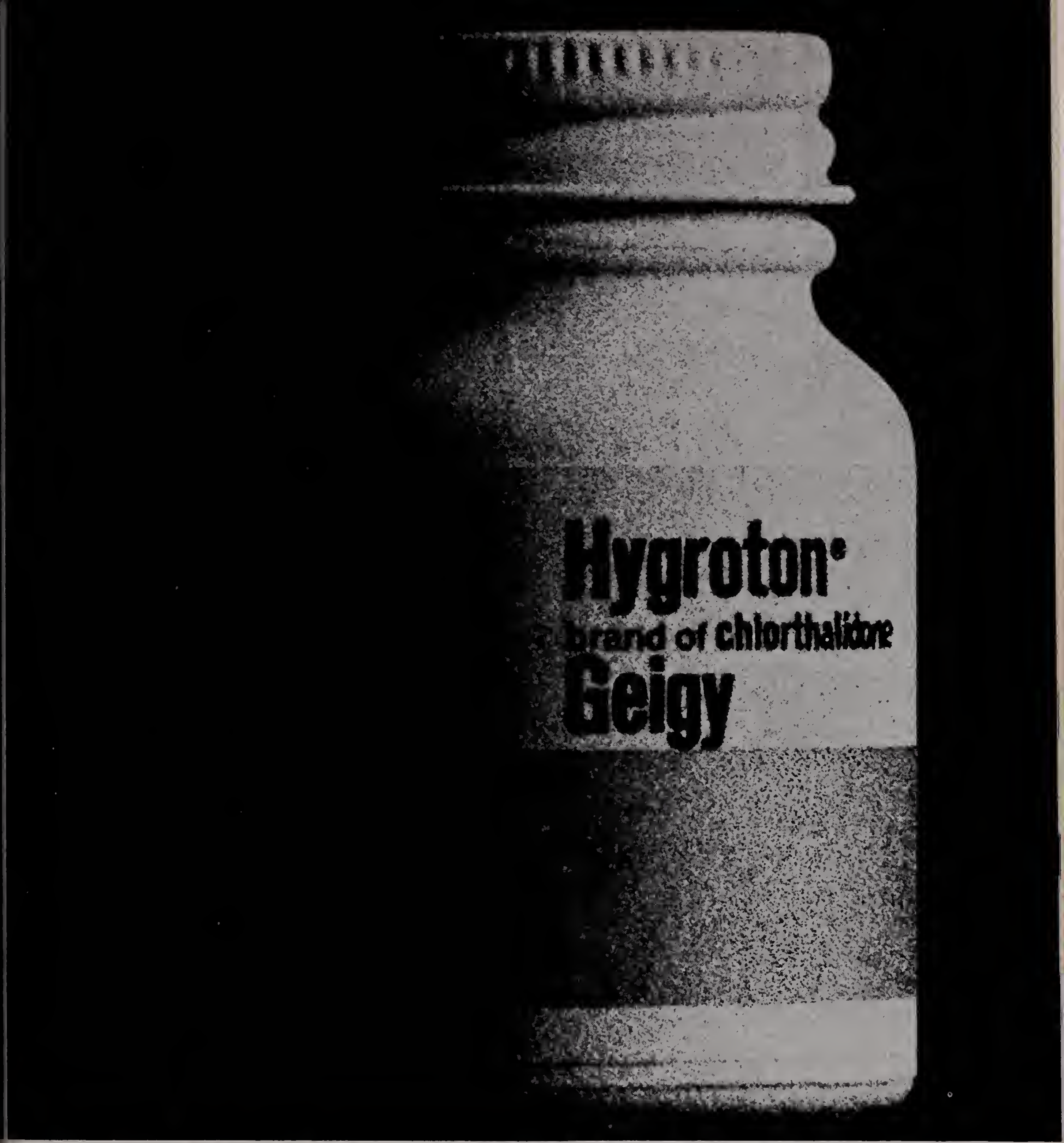

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Patients with edema.
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too young
to be so tired...

revive interest...restore activity promptly with Alertonic®

Each 45 cc. (3 tablespoonfuls) contains: alcohol, 15%; pipradrol hydrochloride, 2 mg.; thiamine hydrochloride (vitamin B_1) (10 MDR*), 10 mg.; riboflavin (vitamin B_2) (4 MDR), 5 mg.; pyridoxine hydrochloride (vitamin B_6), 1 mg.; niacinamide (5 MDR), 50 mg.; choline†, 100 mg.; inositol†, 100 mg.; calcium glycerophosphate, 100 mg. (supplies 2% MDR for calcium and for phosphorus) and 1 mg. each of the following: cobalt (as chloride), manganese (as sulfate), magnesium (as acetate), zinc (as acetate), and molybdenum (as ammonium molybdate).

*Multiple of adult Minimum Daily Requirement supplied.
†The need for these substances in human nutrition has not been established.

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Life *can* begin at forty—except when functional fatigue causes her to feel tired all the time; to start losing interest in friends and surroundings; to look and act older than her years. Alertonic—*a prescription tonic*—can help your patient become her normal self again. Alertonic helps relieve mild depression, revive interest and restore purposeful activity promptly...with a formula that is efficient *and* economical. Alertonic contains a mild central stimulant (pipradrol hydrochloride), 15% alcohol, essential vitamins and minerals. No hormones or MAO-inhibiting drugs are included. No iron. No iodine. One pleasant-tasting tablespoonful before each meal comprises the usual daily dose.

Indications: 1. Functional fatigue such as that often associated with: a depressing life experience or stressful time of life; advancing years; convalescence; limited activity or confinement. 2. Poor appetite and vitamin-mineral deficiency as they occur in: patients having faulty eating habits; geriatric patients who are losing interest in food; patients convalescing from debilitating illness or surgery.

Contraindications: As with other drugs with CNS-stimulating action, Alertonic is contraindicated in hyperactive, agitated or severely anxious patients and in chorea or obsessive-compulsive states.

Side Effects: Reports of overstimulation have been rare. Patients who are known to be unduly sensitive to the effects of stimulant drugs should be observed carefully in the initial stages of treatment.

Dosage: Adults, 1 tablespoonful; children (over 15 years old), 1 to 2 teaspoonfuls; children (4 to 15 years old), 1 teaspoonful. To be taken three times daily 30 minutes before meals.

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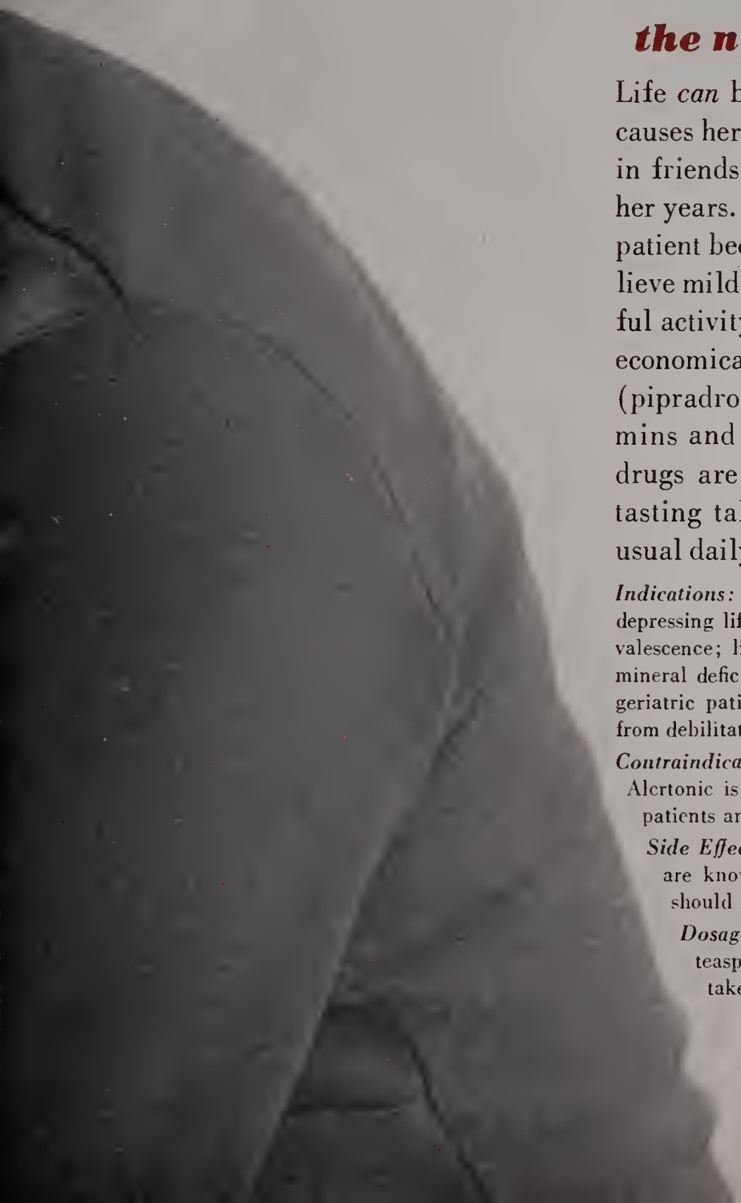

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When the diarrhea sufferer has run the gamut of home remedies without success, pleasant-tasting CREMOMYCIN can answer the call for help. It can be counted on to consolidate fluid stools, soothe intestinal inflammation, inhibit enteric pathogens, and detoxify putrefactive materials—usually within a few hours.

CREMOMYCIN combines the bacteriostatic agents, succinylsulfathiazole and neomycin, with the adsorbent and protective demulcents, kaolin and pectin, for comprehensive control of diarrhea.

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Before prescribing or administering, read product circular with package or available on request.

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where today's theory is tomorrow's therapy

Minnesota Medicine at a Glance

Some Physiology on the Dumping Syndrome — Helft et al. Page 1601

Efforts to explain the cause of the dumping syndrome after a gastric resection have resulted in several theories, namely, the loss of circulating plasma into the intestine; the release of serotonin from the argentaffin cells of the duodenum; and a mechanical theory which suggests that there is distention of the jejunum and duodenum brought about by the introduction of hypertonic materials into the small intestine.

Helft and his co-workers performed some experiments on the animal using 50% glucose instilled into an iliac Thiry-Vella loop. They demonstrated that the concentrated glucose solution abolishes the ability of the iliac mucosa to absorb chlorides, inhibiting its ability to perform osmotic work, and that it also inhibits jejunal motility.

Pigskin Grafts — Bromberg and Song Page 1605

Though heterografts have never been found to be a permanent substitute for skin, recent studies have suggested that heterologous tissue be used as a temporary dressing for large skin defects resulting from burns.

Bromberg and Song have found pigskin to be more suitable for a variety of reasons, and they have observed that the graft is retained for an average of 18 days as against an average of nine days for animal grafts when these were used in animal experiments.

Cerebral Gigantism — Kowlessar Page 1610

The clinical observation of excessive growth in early childhood associated with mental retardation, clumsiness, hypothymism, high arched palate, and precocious sexual development suggests the immediate possibility of cerebral gigantism. Kowlessar provides the details in a case report of this unusual disease in which she found that there were quantitative abnormalities of adrenal hormone production considered to be secondary to the manifest central nervous system disorder.

Dialysis Therapy — Friedman Page 1615

Dialysis therapy is a substitute for the absent or diseased kidney in an effort to remove toxic materials from the blood stream which might otherwise be fatal to the individual.

Peritoneal dialysis as described by Dr. Friedman has been found to be effective in acute tubular necrosis and in prolonged aneuria which was potentially reversible. Although there are some complications associated with peritoneal dialysis, improved techniques and methods to conserve plasma protein will no doubt result in decreased morbidity and mortality.

Hemodialysis has been found effective particularly in drug intoxication.

Megaloblastic Anemia due to Folic Acid Deficiency — Robinson Page 1623

For the description of folic-acid deficiency and an associated megaloblastic anemia, the case report and studies done on this infant clearly delineate the differential features of folic acid and Vitamin B_{12} deficiency. Though the usual daily dose of folic acid has been considered to be from .4 to 10 mg., Robinson has clearly demonstrated that 50 micrograms of pteroylglutamic acid is sufficient to result in a complete cure for this infant's megaloblastic anemia, suggesting that the minimal requirement of folic acid is small.

Replantation of Limbs — Shaftan et al. Page 1645

There have been instances in which replantation of a limb has been successful. Under certain circumstances this procedure can be recommended, though there may be some question as to whether a functionless though viable limb provides enough benefit for a patient to subject himself to the ordeal that follows replantation.

Malignancy of the Female Genitalia — Nelson Page 1651

Carcinoma of the ovaries or an endometrial carcinoma does not respond well to radical pelvic surgery.

In carcinoma of the cervix there are some contraindications to radical surgery, but for the Stage I lesion radiation and radical hysterectomy have been found to be satisfactory, with a survival rate of from 75 to 90 per cent.

Rectal Bleeding — C.P.C. Page 1673

There are not many lesions which cause both rectal pain and bleeding. For evaluation of an interesting clinical path conference, the case history and physical findings can be profitably studied.

Hyperparathyroidism — Rosen et al. Page 1681

There are seven clinical manifestations of hyperparathyroidism but only two are commonly encountered. Renal calculus formations occur in about 70 per cent of the cases and gastrointestinal symptoms in 25 per cent.

The other five clinical manifestations of hyperparathyroidism and the criteria for establishing the diagnosis are detailed in the medical conference.

Lack of Wound Healing — Collagen Synthesis,
Enquist and Adamsons Page 1695

The lack of wound healing and wound disruption may be due to different and unrelated processes. The most important biochemical change occurring in a healing wound is the synthesis and orientation of collagen fibers by fibroblasts. This manuscript reviews the advances that have been made in the study of collagen synthesis which plays an important role in the early phases of wound healing.

It hurts more to have a belief pulled than to have a tooth pulled, and no intellectual novocain is available. — Elmer Davis

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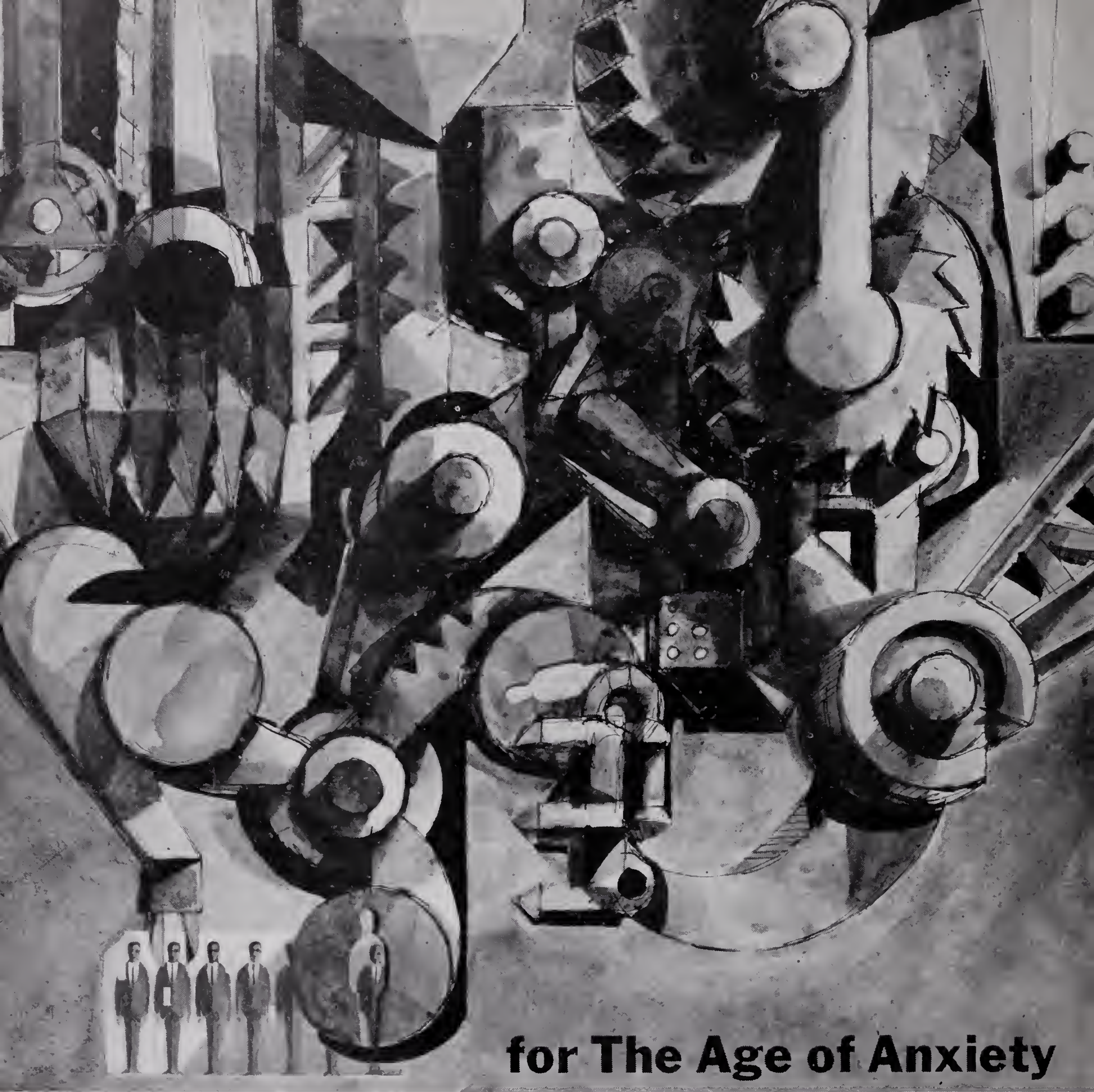
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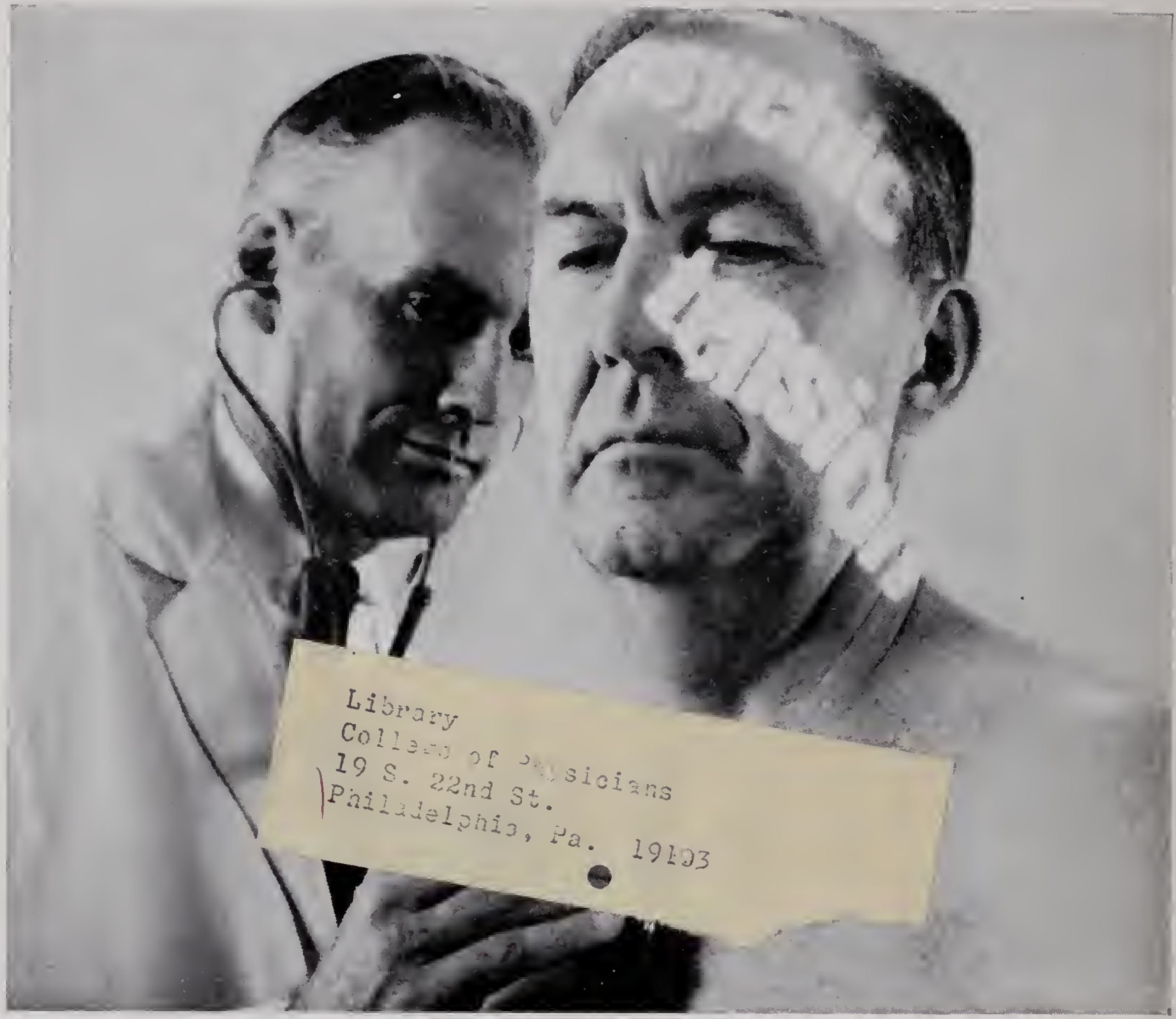

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The Somatic Mask: chest pain—heart disease or psychic tension?

Precordial pain as well as tachycardia, palpitation, breathlessness and faintness or arrhythmias are classic signs of cardiac disease. In many cases, however, they may represent a "somatic mask"—a psychophysiological equivalent of psychic tension.

Valium (diazepam) reduces the patient's disturbing psychic tension and helps improve such related symptoms as sadness and feelings of hopelessness, fatigue, insomnia, crying spells and nervousness.

In prescribing: Dosage — Adults: Mild to moderate psychoneurotic reactions, 2 to 5 mg b.i.d. or t.i.d.; severe psychoneurotic reactions, 5 to 10 mg t.i.d. or q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hrs, then 5 mg t.i.d. or q.i.d. as needed; muscle spasm with cerebral palsy or athetosis, 2 to 10 mg t.i.d. or q.i.d. Geriatric patients: 1 or 2 mg/day initially, increase gradually as needed.

Contraindications: Infants, patients with history of convulsive disorders or glaucoma.

Warning: Not of value in the treatment of psychotic patients, and should not be employed in lieu of appropriate treatment.

Precautions: Limit dosage to smallest effective amount in elderly patients (not more than 1 mg, one or two times daily) to preclude ataxia or oversedation. Advise patients against possibly hazardous procedures until correct maintenance dosage is established; driving during therapy not recommended. In general, concurrent use with other psychotropic agents is not recommended. Warn patients of possible combined effects with alcohol. Safe use in pregnancy not established. Observe usual precautions in impaired renal of hepatic function and in patients who may be suicidal; periodic blood counts and liver function tests advisable in long-term use. Cease therapy gradually.

Side effects: Side effects (usually dose-related) are fatigue, drowsiness and ataxia. Also reported: mild nausea, dizziness, blurred vision, diplopia, headache, incontinence, slurred speech, tremor and skin rash; paradoxical reactions (excitement, depression, stimulation, sleep disturbances and hallucinations) and changes in EEG patterns. Abrupt cessation after prolonged overdosage may produce withdrawal symptoms similar to those seen with barbiturates, meprobamate and chlordiazepoxide HCl.

Supplied: Tablets, 2 mg, 5 mg and 10 mg; bottles of 50.

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Hansen, Olga S.	Minneapolis
Hunt, A. B.	Rochester
Jenson, James E.	Stillwater
Johnson, Douglas	Little Falls
Juergens, Herman M.	Belle Plaine
Kilbride, E. A.	Worthington
Macklin, W. E., Jr.	Litchfield
Martin, D. L.	St. Paul
Sather, E. R.	Alexandria
Skogerboe, R. B.	Karlstad

MEDICINE AND RELIGION

Hermann, Harold W. (Chairman)	Minneapolis
Anderson, Roland G.	Thief River Falls
Barron, Jesse	Minneapolis
Benjamin, Walter	Pipestone
Bergan, Robert O.	Duluth
Hagen, Kristofer	Minneapolis
Holmen, Robert	St. Paul
Lindemann, Charles	Minneapolis
Meinert, John K.	Willmar
Mosser, Donn	Minneapolis
Neils, Vernon	St. Cloud
Scott, Eugene	St. Paul
Sethre, A. E.	Fergus Falls
Spittell, J. A., Jr.	Rochester
Zemke, E. E.	Fairmont

MEMBERSHIP

McCarthy, Donald (Chairman)	Fort Snelling
Lundell, Carl L.	Granite Falls
Onsgard, L. Kenneth	Houston
Richter, D. J.	Virginia
Scott, Eugene E.	St. Paul
Spencer, Robert J.	Rochester
Wallace, M. O.	Duluth

PERMANENT EVALUATION

Carryer, H. M. (Chairman)	Rochester
Davis, Luther F.	Wadena
Fawcett, K. R.	Duluth
Hammar, L. M.	Mankato
Johnson, E. W., Jr.	Rochester
McCarthy, Donald	Fort Snelling
Paulson, Elmer	St. Paul
Virnig, M. P.	Wells
Wasson, L. F.	Alexandria

PHYSICIANS' ASSISTANCE

Blake, James A. (Chairman)	Hopkins
Benjamin, W. G.	Pipestone
Boman, Paul G.	Duluth
Cosgriff, J. A., Sr.	Olivia
Donaldson, C. S.	St. Cloud

PROFESSIONAL LIABILITY

Ritt, A. E. (Chairman)	St. Paul
Carlson, Russel E.	Stillwater
Drexler, George W.	Blue Earth
Gridley, John W.	St. Peter
Jacobson, Clarence	Chisholm
Miller, Harold E.	Minneapolis
Mosby, M. E.	Long Prairie
Wasson, L. F.	Alexandria

PUBLIC HEALTH EDUCATION

Sturley, R. F. (Chairman)	St. Paul

Executive Committee

Christensen, Norman A.	Rochester
Fox, James Rogers	Minneapolis
Semsch, Robert D.	Wayzata
Sturley, R. F.	St. Paul
Wallace, M. O.	Duluth
Williams, George	St. Paul

Councilor District

Donoghue, F. E. (1st)	Rochester
Boone, E. S. (2nd)	Luverne
Flinn, James B. (3rd)	Redwood Falls
Gridley, John W. (4th)	St. Peter
Williams, George (5th)	St. Paul
Fox, James Rogers (6th)	Minneapolis
Murtaugh, Robert J. (7th)	Wadena
Tanquist, Edwin J. (8th)	Alexandria
Wallace, M. O. (9th)	Duluth

PUBLIC HEALTH NURSING

Wilson, Viktor O. (Chairman)	Rochester
Brigham, C. F., Jr.	St. Cloud
Davis, Luther F.	Wadena
Fifer, Ellen Z.	Minneapolis
Fischer, Mario Mc. M.	Duluth
Guy, Jack A.	New London
Knudsen, Helen L.	Minneapolis
Merkert, C. E.	Minneapolis
Schoch, R. B. J.	St. Paul

PUBLIC POLICY

Falls, John L. (Chairman)	Red Wing

Councilor District Chairmen

Spencer, R. J. (1st)	Rochester
Lohmann, John G. (2nd)	Pipestone
Ferguson, W. C. (3rd)	Walnut Grove
Eustermann, J. J. (4th)	Mankato
Richardson, E. J., Jr. (5th)	St. Paul
Blake, James A. (6th)	Hopkins
Luh, Edwin	St. Paul
Fitzsimons, William E. (7th)	Brainerd
Mercil, William F. (8th)	Crookston
Swenson, A. O. (9th)	Duluth

RURAL MEDICAL SERVICE

Nywall, Dean D. (Chairman)	Slayton
Councilor District	
Westrup, John E. (1st)	Lanesboro
Boone, Ervin S. (2nd)	Luverne
Christenson, Carl E. (3rd)	Clinton
Sjostrom, L. E. (4th)	St. Peter
Stratte, A. K. (5th)	Pine City
Anderson, Waldo P. (6th)	Buffalo
Seifert, Donald R. (7th)	Little Falls
Clifford, George W. (8th)	Alexandria
French, Bayard (9th)	Hibbing

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Sheppard, C. G. (Chairman)	St. Peter
Bartholomew, L. G.	Rochester
Engwall, Richard	Minneapolis
Puumala, R. H.	Cloquet
Rutledge, L. H.	Detroit Lakes
Spencer, B. J.	Minneapolis
Wilson, R. H.	Lamoille

STATE HEALTH RELATIONS

Earl, John R. (Chairman)	St. Paul
Bouquet, B. J.	Wabasha
Coe, John I.	Minneapolis
Eustermann, J. J.	Mankato
Grose, Frederick N.	Clarissa
Jackman, R. J.	Rochester
Litman, S. M.	Duluth
Merkert, C. E.	Minneapolis
Simison, Carl	Barnesville
Tesch, Gordon	Elk River
Votel, Thomas W.	St. Paul

UNIVERSITY RELATIONS

Medelman, J. P. (Chairman)	St. Paul
Carryer, H. M.	Rochester
McCarthy, Donald	Fort Snelling
Oppegaard, C. L.	Crookston
Watson, W. H. A.	St. Paul

Councilor Districts

FIRST DISTRICT

W. E. Wellman, M.D. .... Rochester
Counties—Dodge, Fillmore, Goodhue, Houston, Mower, Olmsted, Rice, Steele, Wabasha, Winona.

SECOND DISTRICT

W. B. Wells, M.D. .... Jackson
Counties—Cottonwood, Faribault, Freeborn, Jackson, Martin, Murray, Nobles, Pipestone, Rock, Watonwan.

THIRD DISTRICT

Harold E. Wilmot, M.D. .... Litchfield
Counties—Big Stone, Chippewa, Kandiyohi, Lac Qui Parle, Lincoln, Lyon, Meeker, Pope, Redwood, Renville, Stevens, Swift, Traverse, Yellow Medicine.

FOURTH DISTRICT

J. W. Gridley, M.D. .... St. Peter
Counties—Blue Earth, Brown, Carver, Le Sueur, McLeod, Nicollet, Scott, Sibley, Waseca.

FIFTH DISTRICT

Delmar R. Gillespie, M.D. .... St. Paul
Counties—Anoka, Chisago, Dakota, Isanti, Kanabec, Mille Lacs, Pine, Ramsey, Sherburne, Washington.

SIXTH DISTRICT

O. L. N. Nelson, M.D. .... Minneapolis
Counties—Hennepin, Wright.

SEVENTH DISTRICT

Florian H. Baumgartner .... Albany
Counties—Aitkin, Beltrami, Benton, Cass, Clearwater, Crow Wing, Hubbard, Morrison, Stearns, Todd, Wadena.

EIGHTH DISTRICT

George A. Sather, M.D. .... Fosston
Counties—Becker, Clay, Douglas, Grant, Kittson, Lake of the Woods, Mahnomen, Marshall, Norman, Otter Tail, Pennington, Polk, Red Lake, Roseau, Wilkin.

NINTH DISTRICT

John H. Peterson, M.D. .... Duluth
Counties—Carlton, Cook, Itasca, Koochiching, Lake, St. Louis.

COUNTY MEDICAL ADVISORY COMMITTEES

To County Welfare Boards

AITKIN COUNTY

George Pettersen	Aitkin
F. C. Closuit	Aitkin

ANOKA COUNTY

R. J. Spurzem	Anoka

BECKER COUNTY

E. S. Lorentzen	Detroit Lakes
A. S. Midthune	Lake Park

BELTRAMI COUNTY

D. E. Hoganson	Bemidji
H. A. Palmer	Blackduck

BIG STONE COUNTY

Ray I. Brace	Clinton
Russell Popoff	Graceville
Jacob F. Karn	Ortonville

BLUE EARTH COUNTY

John J. Heimark	Mankato
J. W. Lester	Mapleton
M. W. Dobson	Mankato

BROWN COUNTY

O. B. Fesenmeier	New Ulm
S. J. Kruzich	Sleepy Eye
D. E. Wohlrabe	Springfield

CARLTON COUNTY

R. H. Puumala	Cloquet
Alvan Sach-Rowitz	Moose Lake

CARVER COUNTY

R. D. Pistulka	Chaska
G. T. Schimelpfenig	Chaska
Jon D. Wempner	Waconia

CASS COUNTY

C. R. Pelzl	Pine River
O. F. Ringle	Walker

CHIPPEWA COUNTY

H. A. Roust	Montevideo
L. R. Lima	Montevideo
F. M. Burns	Milan

CHISAGO COUNTY

G. W. Hovde	Chisago City

CLAY COUNTY

J. W. Duncan	Moorhead
V. D. Thysell	Moorhead
C. Simison	Barnesville

CLEARWATER COUNTY

L. J. Larson	Bagley

COOK COUNTY

Roger A. MacDonald	Grand Marais
Wallace R. Smith	Grand Marais

COTTONWOOD COUNTY

H. C. Stratte	Windom
J. H. Dokken	Windom
J. V. Carlson	Westbrook

CROW WING COUNTY

Albertus Dodson	Brainerd
J. B. Nixon	Crosby
George E. Cardle	Brainerd

DAKOTA COUNTY

Bernice Thoreson	South St. Paul
H. J. Just	Hastings
A. H. Field	Savage

DODGE COUNTY

E. A. Olson	Pine Island
D. E. Affeldt	Kasson
Grant E. Olson	West Concord

DOUGLAS COUNTY

G. W. Clifford	Alexandria
J. H. Cain	Alexandria
E. J. Tanquist, Sr.	Alexandria

FARIBAULT COUNTY

John W. Anderson	Blue Earth
R. M. Cullen	Elmore
Donald E. Halvorson	Winnebago

FILLMORE COUNTY

J. E. Westrup	Lanesboro
J. P. Nehring	Preston

FREEBORN COUNTY

C. E. J. Nelson	Albert Lea
A. R. Blumer	Albert Lea
T. M. Hanson	Albert Lea
M. O. Nesheim	Emmons

GOODHUE COUNTY

G. F. Hartnagel	Red Wing
George Hawley, II	Red Wing
R. E. Molenaar	Cannon Falls

GRANT COUNTY

V. A. Doms	Elbow Lake
Alex Webb	Elbow Lake

HENNEPIN COUNTY

M. C. L. Hanson	Minneapolis
J. T. Pewters	Minneapolis
Wayne C. Rydburg	Minneapolis
S. S. Scherling	Minneapolis
Nathan C. Plimpton	Minneapolis
Lester W. Carlander	Minneapolis
George W. Janda, Jr.	Minneapolis
Donald B. Frane	Minneapolis
Harold E. Miller — (Ex-officio)	Minneapolis

HOUSTON COUNTY

Hildegard J. Virnig	Caledonia
Philip Utz	LaCrescent
L. A. Knutson	Spring Grove

HUBBARD COUNTY

Norman R. Haugen	Park Rapids
Gary Baab	Park Rapids

ISANTI COUNTY

R. C. Magnuson	Cambridge

ITASCA COUNTY

V. D. Erickson	Grand Rapids
R. W. Brockway	Grand Rapids
Louis J. Karish	Coleraine

JACKSON COUNTY

V. W. Doman	Lakefield
H. A. Christiansen	Jackson
W. H. Halloran	Jackson

KANABEC COUNTY

E. C. Burseth	Mora

KANDIYOHI COUNTY

H. Bosland	Willmar
L. J. Opsahl	Willmar
R. Carlson	Willmar

KITTSON COUNTY

R. B. Skogerboe	Karlstad

KOOCHICHING COUNTY

George M. Crow	International Falls
Frederick Walter	International Falls

LAC QUI PARLE COUNTY

P. W. Maus	Dawson
Chester A. Anderson	Madison

LAKE COUNTY

Joseph Bloom	Silver Bay
B. F. L'Esperance	Two Harbors

LAKE-OF-THE-WOODS COUNTY

Allen G. Janecky	Baudette

LE SUEUR COUNTY

Dale Bergeron	Le Sueur
R. A. Curtis	Le Center
J. E. Anderson	Le Sueur

LINCOLN COUNTY

C. O. Thompson	Hendricks
M. A. Muesing	Tyler

LYON COUNTY

K. A. Peterson	Marshall
W. Workman	Tracy

MAHNOMEN COUNTY

Charles B. Mercil	Mahnomen

MARSHALL COUNTY

Carle Holmstrom	Warren

MARTIN COUNTY

George N. Kraemer	Fairmont
H. A. Williamson	Fairmont
Anthony Ourada	Fairmont

McLEOD COUNTY

John Smyth	Lester Prairie
G. L. Griebie	Brownton
Kenneth Peterson	Hutchinson

MEEKER COUNTY

G. Olson	Litchfield
Lennox Danielson	Litchfield
W. Nolen	Litchfield

MILLE LACS COUNTY

N. B. Metcalf	Princeton

MORRISON COUNTY

S. W. Watson	Little Falls
D. R. Siefert	Little Falls
R. J. Stein	Pierz

MOWER COUNTY

Harold J. Anderson	Austin

MURRAY COUNTY

J. L. Bader	Slayton
R. F. Pierson	Slayton
H. D. Patterson	Slayton

NICOLLET COUNTY

G. Engstrom	St. Peter
M. E. Lenander	St. Peter

NOBLES COUNTY

R. K. Minge	Worthington
D. E. Nealy	Adrian
E. A. Kilbride	Worthington

NORMAN COUNTY

Clifford Stadem	Twin Valley

OLMSTED COUNTY

Martin Van Herik	Rochester
James Doyle	Rochester
T. O. Wellner	Rochester
Francis J. Kazmier	Rochester
T. T. Myers	Rochester
Maurice Stauffer	Rochester
Richard Steinhilber	Rochester
David Carr	Rochester
J. F. Fairbairn	Rochester

OTTER TAIL COUNTY

Carl J. Lund	Fergus Falls
W. F. Schamber	Parkers Prairie
C. W. Lewis	Henning
L. Syverson	Fergus Falls

PENNINGTON COUNTY

George Martin	Thief River Falls

PINE COUNTY

F. M. Mach	Pine City

PIPESTONE COUNTY

W. G. Benjamin	Pipestone
J. G. Lohmann	Pipestone
G. Beckering	Edgerton

POLK COUNTY

C. G. Uhley	Crookston

POPE COUNTY

Gordon E. Lee	Glenwood
Berton A. Kolp	Glenwood
Foster D. Bucher	Starbuck

RAMSEY COUNTY

Eugene E. Scott	St. Paul
J. L. Sprafka	St. Paul
P. F. W. Rick	St. Paul
E. C. Burklund	St. Paul
J. G. Fee	St. Paul
E. H. Karon	St. Paul
Eva Jane Larson	St. Paul
Alexander McEwan	St. Paul
Ralph Ramlow	St. Paul
R. J. Sells	St. Paul
J. F. Melancon	St. Paul
M. B. Sorem	St. Paul

RED LAKE COUNTY

Vincent Hunt	Red Lake Falls

REDWOOD COUNTY

W. Alcorn	Wabasso
James B. Flinn	Redwood Falls

RENVILLE COUNTY

J. A. Cosgriff, Sr.	Olivia
C. A. Anderson	Hector

RICE COUNTY

A. W. Nuetzman	Faribault
Bernard Street	Faribault

ROCK COUNTY

C. L. Sherman	Luverne
A. C. Martin	Luverne
F. W. Bofenkamp	Luverne
E. S. Boone	Luverne
D. M. Odland	Luverne

ROSEAU COUNTY

Jack Delmore	Roseau

ST. LOUIS COUNTY

J. J. Dwyer	Duluth
F. W. Conley	Duluth
J. P. Knoedler	Duluth
Kenneth Ahola	Hibbing
Richard Barnes	Aurora
Clarence Jacobson	Chisholm
H. Wayne Johnston	Virginia
Bernard Halper	Hibbing
Harrison E. Law	Virginia

SCOTT COUNTY

H. M. Juergens	Belle Plaine
C. F. Cervenka	New Prague
J. E. Ponterio	Shakopee

SHERBURNE COUNTY

G. H. Tesch	Elk River

SIBLEY COUNTY

G. O. Greene	Arlington

STEARNS-BENTON COUNTY

L. A. Loes	St. Cloud
L. B. Kuhlmann	Melrose
R. Jones	St. Cloud
W. A. Autrey	St. Cloud
D. C. Heckman	St. Cloud

COUNTY MEDICAL ADVISORY COMMITTEES

STEELE COUNTY

R. W. deWerd	Owatonna
K. G. Henry	Owatonna
C. W. Lundquist	Owatonna

STEVENS COUNTY

R. A. Rossberg	Morris
O. A. Eide	Hancock

SWIFT COUNTY

R. Nelson	Benson
Joseph Rorem	Appleton
N. Wagner	Benson

TODD COUNTY

M. E. Mosby	Long Prairie
F. N. Grosse	Clarissa

TRAVERSE COUNTY

A. E. Magnuson	Wheaton
A. L. Lindberg	Wheaton
H. C. Winge	Wheaton

WABASHA COUNTY

W. P. Gjerde	Lake City
D. W. Sontag	Lake City
J. R. Flatt	Wabasha

WADENA COUNTY

L. T. Davis	Wadena
W. E. Parker	Sebeka
W. B. Halme	Wadena

WASECA COUNTY

Wayne Campbell	Waseca
Laddie E. Stover	Waseca

WASHINGTON COUNTY

J. E. Jenson	Stillwater
R. E. Carlson	Stillwater

WATONWAN COUNTY

A. D. Mattson	St. James
Herbert Boysen	Madelia

WILKIN COUNTY

L. O'Brien	Breckenridge
C. W. Jacobson	Breckenridge
Neil Kippen	Breckenridge

WINONA COUNTY

Herbert vR. Heise	Winona
Robert B. Tweedy	Winona
Henry J. Roemer	Winona

WRIGHT COUNTY

S. J. Raetz	Maple Lake
R. M. Sandeen	Buffalo

YELLOW MEDICINE COUNTY

C. L. Lundell	Granite Falls
Olin M. Odlund	Granite Falls
E. R. Hudec	Echo

Woman's Auxiliary to the Minnesota State Medical Association

Officers

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Mrs. G. R. Diessner	President-elect	Rochester
Mrs. E. Hudec	First Vice President	Echo
Mrs. W. P. Gjerde	Second Vice President	Lake City
Mrs. Elmer Hill	Third Vice President	Minneapolis
Mrs. R. P. Buckley	Fourth Vice President	Duluth
Mrs. Cyril Tifft	Recording Secretary	St. Paul
Mrs. Harry S. Proud	Corresponding Secretary	St. Paul
Mrs. L. A. Laikola	Treasurer	Adrian
Mrs. John H. Peterson	Auditor	Duluth
Mrs. Ralph Olsen	Historian	St. Paul
Mrs. W. P. Gardner	Parliamentarian	St. Paul

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Mrs. R. K. Minge	Second District	Worthington
Mrs. Norval Westby	Third District	Madison
Mrs. R. D. Hottinger	Fourth District	Janesville
Mrs. S. M. Loken	Fifth District	St. Paul
Mrs. Karl W. Anderson	Sixth District	Excelsior
Mrs. R. T. Petersen	Seventh District	St. Cloud
Mrs. J. F. Knapp	Eighth District	Detroit Lakes
Mrs. F. W. Conley	Ninth District	Duluth

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By-Laws—Mrs. Theodore Fritsche	New Ulm
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Mrs. Dean D. Nywall (Co-Chairman)	Slayton
Disaster Preparedness—Mrs. L. L. Bissinger	Brainerd
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Health Careers—Mrs. Ellery James	Mahtomedi
International Health Activities—	
Mrs. Carl D. Eklund	Duluth
Mental Health—Mrs. F. E. Ellison	Monticello
Safety and Rural Health—	
Mrs. Grant F. Hartnagel	Red Wing
Finance—Mrs. Leo Fink	Minneapolis
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AMA-ERF—Mrs. M. I. Shelander	St. Paul
Legislation—Mrs. Winston Lindberg	Wayzata
Membership—Mrs. G. R. Diessner	Rochester
Editor—Gopher Doctor's Wife—	
Mrs. F. G. Gunlaugson	Minneapolis
Press and Publicity—	
Mrs. Thomas B. Merner	Minneapolis
Resolutions—Mrs. Charles S. Donaldson	St. Cloud
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Mrs. T. Seery	Austin
Mrs. Robert Murray	Hibbing
Mrs. A. H. Borgerson	Long Prairie
Mrs. W. E. Fitzsimons	Brainerd
Special Committee—Job Analysis Handbook—	
Mrs. M. I. Hauge	Clarkfield
Fall School of Instruction and Mid-Winter Board Meeting—	
Mrs. Elmer Paulson	St. Paul
Mrs. Harry Hall	Minneapolis
Advisory Committee—	
Mrs. Karl Johnson	Duluth
Mrs. H. H. Fesler	St. Paul
Mrs. L. P. Howell	Rochester
Mrs. R. F. Erickson	Minneapolis
Mrs. M. I. Hauge	Clarkfield

County Medical Society Roster

KEY TO SYMBOLS AS FOLLOWS

*	Deceased
†	Affiliated, Associate, Life, or Resident Members
#	Service
‡	Wife is Member of Woman's Auxiliary
¶	Honorary Member

BLUE EARTH COUNTY MEDICAL SOCIETY

Blue Earth County
Regular meetings, last Monday of the month
Annual meetings December
Number of members 62

	PRESIDENT	
	Setzer, Hobert J., Jr.	Mankato
	SECRETARY	
	Gislason, Paul H.	Mankato
‡	Anderson, Oscar D.	Mankato
‡	Arnesen, Paul M.	Mankato
‡	Batdorf, B. Niles	Mankato
†	Butzer, John A.	Mankato
	Butzer, John F.	Mankato
‡	Chalgren, William S.	Mankato
‡	Conley, Robert H.	Mankato
	Dobson, Mervin W.	Mankato
	Eustermann, John J.	Mankato
‡	Engstrom, Robert B.	Mankato
‡	Finch, J. E.	Mankato
	Flentje, Dale E.	Mankato
‡	Florine, Martin C.	Mankato
‡	Fortier, Rene G.	Mankato
†	Franchere, Frederick W.	Lake Crystal
‡	Freeman, Donald H.	Mankato
‡	Geurs, Benjamin R.	Mankato
‡	Gislason, Paul H.	Mankato
‡	Hammar, Lawrence M.	Mankato
	Hankerson, Robert G.	Minnesota Lake
‡	Heimark, John J.	Mankato
‡	Heller, Edgar E.	Mankato
‡	Hoeper, Philip G.	Mankato
‡	Howard, Marshall I.	Mankato
	Huffington, Herb L.	Waterville
†	Huffington, Herbert L.	Lutsen
‡	Jones, Orville H.	Mankato
†	Juliar, Richard O.	Los Angeles, California
‡	Kaufman, Walter B.	Mankato
‡	Kearney, R. Wynn	Mankato
†	Kemp, Alphonse F.	Mankato
	Lester, John W.	Mapleton
*†	Liedloff, Adolph G.	Mankato
‡	Lindblom, Alton E.	North Mankato
†	Luck, Hilda	Mankato
‡	Lund, J. Benjamin	Mankato
	Marso, John L.	Mankato
‡	Mathews, Wallace E.	Mankato
‡	Meredith, Donald C.	Mankato
‡	Mickelson, John C.	Mankato
†	Miller, Victor I.	Belmont, California
‡	Morgan, Hugh O.	Amboy
‡	Olive, John T., Jr.	Mankato
‡	Penn, George E.	Mankato
‡	Roth, Frederick D.	Mankato
‡	Sanford, Raymond A.	Mankato
‡	Scheidel, Alois M.	Mankato
‡	Schlossberg, Victor E., Jr.	Mankato
*†	Schmidt, Paul A.	Aurora, Oregon
‡	Schmitz, Anthony A.	Mankato
‡	Setzer, Hobert J., Jr.	Mankato
‡	Sherrill, Gene D.	Mankato
‡	Sjoding, J. Donald	Mankato
‡	Smith, Harry J.	Lake Crystal
‡	Smith, Paul M.	Lake Crystal
‡	Snider, Howard R.	Mankato
‡	Stillwell, Walter C.	Mankato
‡	Strobel, Claire J.	Mankato
‡	Swenson, Donald B.	Mankato
‡	Thiem, Chester E.	Mankato
†	Troost, H. Bradley	Mankato
†‡	Vezina, John C.	Mapleton
‡	Von Drasek, Joseph	Mankato
†‡	Wentworth, Albert J.	Mankato

BLUE EARTH VALLEY MEDICAL SOCIETY

Martin, Watonwan and Faribault Counties
Regular meetings, third Wednesday of each month
Annual meeting in November
Number of members 43

	PRESIDENT	
	John W. Anderson	Blue Earth
	SECRETARY	
	Boysen, Herbert	Madelia
‡	Anderson, John W.	Blue Earth
	Armstrong, Ralph S.	Winnebago
	Barr, James S.	New York, New York
‡	Bellomo, John	Fairmont
‡	Bergman, Oscar B.	St. James
‡	Boysen, Herbert	Madelia
†‡	Bratrude, Earl J.	St. James
	Cox, Russell L.	Estherville, Iowa

Continued on Next Page

Blue Earth Valley Medical Society (Continued)

	Cullen, Robert M.	Elmore
‡	Drexler, George W.	Blue Earth
‡	Feigal, William M.	Fairmont
‡	Gardner, Jack K.	Fairmont
†‡	Gardner, Victor H.	Fairmont
	Halverson, Donald E.	Winnebago
‡	Halverson, William G.	Madelia
‡	Hanson, Lewis	Frost
‡	Hruza, William J.	Madelia
†	Hunt, Roscoe C.	Fairmont
	Kraemer, George N.	Fairmont
‡	Krause, Carl W.	Fairmont
‡	Lester, Malcolm J., Jr.	Truman
	Lindahl, Merlyn J.	Sherburn
	Louisell, Charles T.	Fairmont
‡	Mattson, Albert D.	St. James
	Mills, John L.	Winnebago
‡	Moulton, Keith B.	St. James
‡	Nickerson, John R.	Fairmont
‡	Nickerson, Neil D.	Fairmont
‡	Ourada, Anthony L.	Fairmont
‡	Parson, R. A.	St. James
	Parsons, Ralph L.	Trimont
‡	Russ, Homer H.	Blue Earth
‡	Schulz, Robert W.	Fairmont
‡	Smith, Don V.	Blue Earth
‡	Snyder, Clifford D.	Kiester
‡	Thayer, Ellsworth A.	Fairmont
‡	Vaughan, Victor M.	Truman
‡	Virnig, Mark P.	Wells
‡	Virnig, Richard P.	Wells
‡	Wandke, Otto E.	Fairmont
‡	Watkins, John A.	Wells
‡	Williamson, Harold A.	Fairmont
*†	Wilson, Clyde E.	Blue Earth
‡	Zemke, Erhart E.	Fairmont

BROWN COUNTY MEDICAL SOCIETY

Brown County
Regular meetings January, April, October
Annual meeting in January
Number of members 26

	PRESIDENT	
	Kruzich, Stephen J.	Sleepy Eye
	SECRETARY	
	Wohlrabe, Donald E.	Springfield
‡	Black, William A.	New Ulm
‡	Boyle, Francis J.	Springfield
‡	Burnett, Joseph W.	New Ulm
‡	Cairns, Robert J.	Redwood Falls
‡	Carthey, Frank J.	New Ulm
‡	Fesenmaier, Otto B.	New Ulm
†	Fritsche, Albert	New Ulm
‡	Fritsche, Carl J.	New Ulm
‡	Fritsche, Theodore R.	New Ulm
	Goblirsch, Andrew P.	Sleepy Eye
*	Hovde, Rolf	Winthrop
‡	Johnson, Rex R.	New Ulm
‡	Kaiser, Milton L.	New Ulm
‡	Keithahn, Elmer E.	Sleepy Eye
‡	Kitzberger, Peter J.	New Ulm
‡	Kruzich, Stephen J.	Sleepy Eye
†	Kusske, Arthur L.	New Ulm
	Muesing, William J.	New Ulm
†	Nuessle, Walter G.	Springfield
‡	Penk, Engward L.	Springfield
	Peterson, Roy A.	Vesta
‡	Rimas, Matthew J.	Comfrey
‡	Ringhofer, Lawrence	New Ulm
‡	Saffert, Cornelius A.	New Ulm
*	Seifert, Otto J.	New Ulm
‡	Vogel, Howard A. L.	New Ulm
‡	Wohlrabe, Donald E.	Springfield
‡	Wohlrabe, Edwin J.	Springfield

CAMP RELEASE DISTRICT MEDICAL SOCIETY

Chippewa, Lac qui Parle and Yellow Medicine Counties
Regular meetings, second Thursday of each month except
July and August
Annual meeting, November
Number of members 29

	PRESIDENT	
	Burns, F. M.	Milan
	SECRETARY	
	Hagberg, Norman L.	Montevideo
‡	Allen, John H.	Montevideo
	Anderson, Chester A.	Madison
‡	Boody, George J., Jr.	Cambridge
‡	Burns, Floyd M.	Milan
†	Burns, M. A.	Milan
‡	Camp, Ray J	Madison
†	Fallon, Virgil T.	Minneapolis
‡	Gustafson, Robert W.	Granite Falls
‡	Hagberg, Norman L.	Montevideo
‡	Hauge, Malvin I.	Clarkfield
†	Holmberg, LeRoy J.	Canby
‡	Hudec, Elwyn R.	Echo
‡	Johnson, Vilhelm M.	Dawson
†	Jordan, Kathleen B. Smith	Granite Falls
	Jordan, Lewis S.	Granite Falls
†‡	Kaufman, William C.	Appleton
‡	Kremer, Jerome L.	Montevideo
‡	Lima, Ludvig R.	Montevideo
‡	Lundell, Carl L.	Granite Falls
‡	Maus, Philip W.	Dawson
‡	Niazi, Suad A.	Granite Falls
‡	Odland, Olin M.	Granite Falls
‡	Owens, William A.	Montevideo
†	Pertl, Albert L.	Canby
‡	Radke, Robert L.	Montevideo
‡	Roust, Henry A.	Montevideo
‡	Schmidt, Paul G.	Granite Falls
‡	Westby, Norval M.	Madison

CLAY-BECKER COUNTY MEDICAL SOCIETY

Clay and Becker Counties
Regular meetings, three per year
Annual meeting, December
Number of members 30

	PRESIDENT	
	Duncan, James W.	Moorhead
	SECRETARY	
	Odland, M. E.	Detroit Lakes
‡	Bigler, Earl E.	Perham
	Bigler, Ivan E.	Perham
	Bologna, Camillo V.	Moorhead
†	Bottolfson, B. T.	Moorhead
	Brenk, Paul E.	Detroit Lakes
	Carlon, Donald L.	Moorhead
‡	Carlson, Vernon J.	Moorhead
‡	Dodds, William C.	Detroit Lakes
‡	Duncan, James W.	Moorhead
‡	Geib, Marvin J.	Fargo, North Dakota
†	Hagen, Olaf J.	Moorhead
‡	Holten, John	Moorhead
†‡	Houglum, Arvid J.	St. Paul
	Johnson, Olga H.	Moorhead
	Knapp, James F.	Detroit Lakes
	Koons, William R.	Mahnomen
‡	Larson, Arnold	Detroit Lakes
‡	Lorentzen, Ernest S.	Detroit Lakes
‡	Midthune, Andreen S.	Lake Park
‡	Moberg, Clarence W.	Detroit Lakes
‡	Odland, Mark E.	Detroit Lakes
*†	Otto, Henry C.	Frazee
	Reeber, Erick	Bagley
‡	Rice, Hagbart G.	Moorhead
‡	Rutledge, John B.	Detroit Lakes
†‡	Rutledge, Lloyd H.	Detroit Lakes
	Saxman, Gertrude E.	Ulen
‡	Simison, Carl	Barnesville
	Thysell, Vernon D.	Moorhead
‡	Watson, Robert N.	Detroit Lakes
‡	Watson, Virgil A.	Detroit Lakes

EAST CENTRAL MINNESOTA MEDICAL SOCIETY

Anoka, Chisago, Isanti, Kanabec, Mille Lacs, Pine and Sherburne Counties
Regular meetings first Tuesday of even months of the year
Annual meeting First Tuesday in December
Number of members 42

	PRESIDENT	
	Mach, Ralph F.	Pine City
	SECRETARY	
	Sommer, Robert K.	Elk River
‡	Adkins, Galen H.	Cambridge
	Ahlstrom, Robert C.	Braham
	Berge, Harry L.	Mora
‡	Berglund, Alvin E.	Cambridge
	Bunker, Bevan W.	Anoka
‡	Burseth, Edgar C.	Mora
	Courteau, Robert D.	Onamia
‡	Deason, Keith B.	Chisago City
‡	Dittrich, R. J.	Cambridge
	Gailitis, Veronika M.	St. Paul
	Grinvalds, Anna O.	Cambridge
	Halpin, Joseph E.	Rush City
	Henry, Harold W.	Hinckley
‡	Hilgedick, William R.	Chisago City
*	Holmes, Alva E.	Rush City
‡	Hovde, Gordon W.	Chisago City
	Huber, Robert W.	St. Croix Falls, Wis.
	Hubin, Edwin G.	Sandstone
	Johnson, Aldridge F.	Isle
‡	Kapsner, Alfred	Princeton
†	Kelsey, Carleton G.	St. Paul
‡	Larson, Gerald E.	Cambridge
	Lindquist, Dale C.	Lindstrom
‡	McManus, William F.	Princeton
‡	Mach, Ralph F.	Pine City
‡	Magnuson, Raymond C.	Cambridge
	Metcalf, Norman B.	Princeton
	Nelson, Luther A.	Rush City
‡	Nordman, Willard F.	Mora
	Nygren, William T.	Braham
	Peterson, Alvin C.	Mora
	Popovich, Dragojla	Milwaukee, Wis.
‡	Roehlke, Arthur B.	Elk River
‡	Sander, John L.	Cambridge
†	Schut, John W.	Minneapolis
‡	Seecamp, Carsten H.	Cambridge
	Sommer, Robert K.	Elk River
	Spurzem, Raymond J.	Anoka
‡	Stratte, Alf K.	Pine City
‡	Swenson, Roy G.	North Branch
‡	Tesch, Gordon H.	Elk River
‡	Travis, Richard C.	Elk River
†	Waller, Joseph D.	Pine City

FREEBORN COUNTY MEDICAL SOCIETY

Freeborn County
Regular meetings, third Thursday of even-numbered months
Annual meeting, December
Number of members 35

	PRESIDENT	
	Gamble, E. J.	Albert Lea
	SECRETARY	
	Ellertson, Leonard M.	Albert Lea
	Arnold, Arthur L.	Albert Lea
‡	Barr, Lowell C.	Albert Lea
‡	Barr, Lowell W.	Albert Lea
‡	Bartness, John E.	Albert Lea
‡	Blumer, Arlo R.	Albert Lea
‡	Bryant, Emmett P.	Ellendale
†	Burns, Catherine	Excelsior

Continued on Next Page

Freeborn County Medical Society (Continued)

†	Butturff, Carl R.	Freeborn
†	Calhoun, Frank W.	Albert Lea
	Cole, George A.	Albert Lea
‡	Demo, Robert A.	Albert Lea
‡	Donovan, Daniel L.	Albert Lea
‡	Egge, Sanford G.	Albert Lea
‡	Ellertson, Leonard M.	Albert Lea
‡	Erdal, Ove A.	Albert Lea
†	Freeman, John P.	Glenville
‡	Gamble, Elbert J.	Albert Lea
‡	Gill, Theodore M.	Albert Lea
‡	Hansen, Theodore M.	Albert Lea
‡	Holian, Darwin K.	Albert Lea
†	Kassa, Lawrence J.	Albert Lea
‡	Keil, Marcus A.	Albert Lea
†	Leopard, Brand A.	Brownsville, Texas
‡	Menefee, Edward C.	Albert Lea
	Myers, Theodore P.	Albert Lea
‡	Neel, Harry B.	Albert Lea
‡	Nelson, Clayton E. J.	Albert Lea
‡	Nesheim, Martin O.	Emmons
‡	Palmer, Clinton F.	Albert Lea
‡	Schmidt, Ruben F.	Alden
‡	Sherman, Alfred G.	Albert Lea
‡	Steiner, Leon E.	Albert Lea
‡	Stoker, Lynn C.	Albert Lea
‡	Whitson, Sidney A.	Albert Lea
‡	Wilcox, G. Charles	Albert Lea

GOODHUE COUNTY MEDICAL SOCIETY

Goodhue County
Regular meeting, April
Annual meeting, October
Number of members 26

PRESIDENT		
	Douglass, Jesse E.	Cannon Falls
SECRETARY		
	Rayner, Ralph R.	Red Wing
†	Aanes, Almer M.	Red Wing
‡	Akins, Willard M.	Red Wing
†‡	Billings, Harry H.	Red Wing
‡	Brusegard, James F.	Red Wing
‡	Cant, Wilbur F.	Red Wing
‡	Delahunty, John R.	Red Wing
	Douglass, Jesse E.	Cannon Falls
	Falls, John L.	Red Wing
†‡	Graves, Richard B.	Red Wing
‡	Halvorson, James W.	Zumbrota
‡	Hartnagel, Grant F.	Red Wing
‡	Hawley, George M. B., II	Red Wing
‡	Jackish, George E.	Red Wing
‡	Juers, Edward H.	Red Wing
‡	Larson, Oliver E. H.	Zumbrota
‡	Liffrig, William W.	Red Wing
	Molenaar, Robert E.	Cannon Falls
‡	Rayner, Ralph R.	Red Wing
‡	Schroeder, Glenn E.	Red Wing
‡	Shepard, Richard	Red Wing
‡	Sherman, Royal V.	Red Wing
†	Smith, Myron W.	Red Wing
‡	Steffens, Leon A.	Red Wing
‡	Walter, William E.	Wanamingo
‡	Wasmund, Clarence W.	Red Wing
‡	Williams, Marland R.	Cannon Falls

HENNEPIN COUNTY MEDICAL SOCIETY

Hennepin County
Regular meetings, first Monday of the Months of
October, January, March and May, except when
otherwise designated
Annual meeting, first Monday in October
Number of members 1252

PRESIDENT		
	Hall, Harry B.	Minneapolis
SECRETARY		
	Chisholm, Tague C.	Minneapolis
EXECUTIVE SECRETARY		
	Cook, Thomas P.	Minneapolis
‡	Abramson, Burton I.	Minneapolis
	Abramson, Milton	Minneapolis
‡	Abullarade, Jose A.	Minneapolis
	Adcock, Leon L.	Minneapolis
‡	Adkins, C. Douglas	Minneapolis
‡	Agustsson, Hreidar	Minneapolis
‡	Ahern, Eugene E.	Minneapolis
	Alari, Heino	Minneapolis
‡	Alexander, Harlan A.	Minneapolis
‡	Aling, Charles A.	Minneapolis
‡	Allen, James R.	Minneapolis
	Alter, Milton	Minneapolis
†	Altnow, Hugo O.	Coral Gables, Florida
‡	Amatuzio, Donald S.	Minneapolis
‡	Amren, Don P.	Minneapolis
	Anderegg, Alfred F.	St. Paul
‡	Andersen, James G.	Minneapolis
‡	Anderson, Arnold S.	Minneapolis
	Anderson, Ben H.	Minneapolis
‡	Anderson, David M.	Minneapolis
†	Anderson, Edward D.	Vaud, Switzerland
‡	Anderson, Ernest R.	Minneapolis
‡	Anderson, Frank J.	Minneapolis
	Anderson, John A.	Minneapolis
‡	Anderson, Karl W.	Minneapolis
	Anderson, Richard W.	Minneapolis
	Anderson, Roger E.	Minneapolis
‡	Anderson, Roger L.	Minneapolis
	Anderson, Thomas P.	Minneapolis
‡	Anderson, U. Schuyler	Fargo, North Dakota
	Anderson, Wallace E.	Minneapolis
‡	Anderson, Wallace R.	Minneapolis
‡	Anderson, William H.	Minneapolis
‡	Anderson, William T.	Minneapolis
†	Andreassen, Einar C.	Minneapolis
‡	Andreassen, Rolf L.	Minneapolis
‡	Andreasen, Karl d'A	Minneapolis

Hennepin County Medical Society (Continued)

‡	Ankner, Frank J.	Minneapolis
‡	Anonsen, Richard E.	Minneapolis
	Anselment, Lois A.	Excelsior
†	Arends, Archabald L.	Minneapolis
‡	Arey, Stuart Lane	Minneapolis
‡	Arhelger, Stuart W.	Minneapolis
‡	Arlander, Clarence E.	Minneapolis
‡	Arling, Leonard S.	Minneapolis
‡	Arms, James J.	Minneapolis
	Armstrong, Byron H.	Minneapolis
	Arnold, Ann W.	Minneapolis
	Arnold, Thomas B.	Minneapolis
†	Arvidson, Carl G.	Minneapolis
‡	Aughenbaugh, John W.	Minneapolis
	Azad, A. M.	Minneapolis
‡	Baggenstoss, Osmond J.	Minneapolis
‡	Bagley, Russell W.	Minneapolis
	Bah, Merle C.	St. Paul
‡	Baken, Melvin P.	Minneapolis
‡	Baken, Melvin P., Jr.	Minneapolis
	Baker, Abe B.	Minneapolis
†	Baker, Alfred T.	Minneapolis
	Baker, C. Camak	Minneapolis
‡	Baker, Milton E.	Minneapolis
	Bakke, Arnold C.	Minneapolis
‡	Baleisis, Peter	Minneapolis
‡	Balkin, Samuel G.	Minneapolis
‡	Balogh, Charles J.	Minneapolis
	Bank, Harry E.	Minneapolis
‡	Barnett, Robert M.	Minneapolis
‡	Barno, Alex	Minneapolis
‡	Barr, Maxwell M.	Minneapolis
	Barr, Robert M.	Minneapolis
	Barrett, Patrick J.	Minneapolis
	Barron, Jesse J.	Minneapolis
†‡	Barron, Moses	Beverly, Hills, Calif
	Beach, Northrop	Minneapolis
	Beard, Archibald H., Jr.	Minneapolis
‡	Beirstein, Samuel	Minneapolis
‡	Beiswanger, Richard H.	Minneapolis
‡	Bell, Donald C.	Minneapolis
‡	Bellville, Titus P.	Minneapolis
‡	Belzer, Meyer S.	Minneapolis
#	Bendel, Richard P.	San Francisco, California
	Benesh, Louis A.	Minneapolis
‡	Benjamin, Edwin G.	Minneapolis
‡	Benjamin, Harold G.	Minneapolis
	Benjamin, Richard D.	Minneapolis
‡	Benjamin, Robert B.	Minneapolis
	Bentz, Herman D.	Anoka
	Berg, Clinton C.	Excelsior
	Berger, Alex G.	Minneapolis
‡	Bergh, George S.	Minneapolis
	Bergh, Solveig M.	Minneapolis
‡	Berglund, Eldon B.	Minneapolis
‡	Bergquist, James R.	Minneapolis
‡	Berkwitz, Nathaniel J.	Minneapolis
	Berman, David A.	Minneapolis
	Berman, Reuben	Minneapolis
	Bernstein, Irving C.	Minneapolis
‡	Berris, Harold	Minneapolis
‡	Berry, Ronald N.	Minneapolis
‡	Bessesen, Alfred N.	Minneapolis
‡	Bevis, William D.	Minneapolis
	Bieter, Raymond N.	Minneapolis
‡	Bilka, Paul J.	Minneapolis
‡	Binder, Manuel R.	Minneapolis
	Bittick, Wilbur H.	Minneapolis
‡	Blackard, Clyde E.	Minneapolis
‡	Blake, Allan J.	Hopkins
‡	Blake, James A.	Hopkins
‡	Blake, Paul S.	Minneapolis
	Blaw, Michael E.	Minneapolis
‡	Bloch, Henry S.	Minneapolis
‡	Bloedel, Traugott J.	Osseo
‡	Blomberg, Robert D.	Minneapolis
‡	Bloom, David	Minneapolis
‡	Bloom, Norman B.	Minneapolis
	Blumenthal, Malcolm N.	Minneapolis
‡	Bofenkamp, Benjamin	Minneapolis
‡	Bohn, Donald G.	Minneapolis
‡	Boies, Lawrence R.	Minneapolis
‡	Borman, Chauncey N.	Minneapolis
‡	Borowicz, Leonard A.	Minneapolis
	Bouthilet, Florence J.	Minneapolis
‡	Bowers, Gordon G.	Minneapolis
‡	Bowlin, Paul F.	Minneapolis
†	Boynton, Ruth E.	Miami, Florida
	Bradley, Jeanne B.	Minneapolis
	Bradley, John G.	Minneapolis
	Brandt, Henry E.	Minneapolis
	Bransford, Paul W.	Minneapolis
†‡	Bratrud, Arthur F.	Minneapolis
‡	Braun, Rene	Minneapolis
‡	Brauti, E. Fred	Minneapolis
	Breitenbucher, Robert B.	Minneapolis
‡	Brekke, Harvey J.	Minneapolis
‡	Brennan, Joseph G.	Minneapolis
	Brill, Alice K.	Minneapolis
†	Brooks, Charles N.	Minneapolis
	Brown, John H.	Minneapolis
	Brown, William D.	Minneapolis
	Brown, William D., Jr.	Minneapolis
‡	Buchstein, Harold F.	Minneapolis
‡	Buckley, Joseph J.	Minneapolis
	Bugenstein, Robert H.	Minneapolis
	Buie, Louis A., Jr.	Minneapolis
‡	Buirge, Raymond E.	Minneapolis
‡	Bundt, Robert E.	Minneapolis
‡	Burnham, Wesley H.	Minneapolis
‡	Bushard, Wilfred J.	Phoenix, Ariz.
*‡	Buzzelle, Leonard K.	Minneapolis
‡	Cable, Morris L.	Minneapolis
‡	Cabot, Clyde M.	Minneapolis
‡	Calin, S. Hartley	Minneapolis
†	Cameron, Isabell L.	Minneapolis
‡	Campbell, Orwood J.	Minneapolis
‡	Caplan, Leslie	Minneapolis
‡	Card, William H.	Minneapolis
	Cardle, James G.	Minneapolis
‡	Cardle, John B.	Minneapolis
‡	Carey, James B., Jr.	Minneapolis
‡	Carlander, Lester W.	Minneapolis
‡	Carlson, Charles V.	Mound
‡	Carlson, Lawrence	Minneapolis
‡	Carlson, Leonard T.	Minneapolis
‡	Caron, Robert P.	Minneapolis
	Carr, William J.	Minneapolis
‡	Caspers, Carl G.	Minneapolis
‡	Cauble, Charles F.	Minneapolis
†‡	Cavanor, Frank T.	Minneapolis
‡	Ceder, Elmer T.	Minneapolis
‡	Cella, Joseph A.	Minneapolis
‡	Chadbourn, Wayne A.	Minneapolis
	Challman, S. Alan	Minneapolis
	Chandler, William M.	Minneapolis

Continued on Next Page

Hennepin County Medical Society (Continued)

‡	Chedister, Charles R.	Minneapolis
‡	Chesler, Merrill D.	Minneapolis
	Child, Sherman B.	Minneapolis
‡	Chisholm, Tague C.	Minneapolis
	Chou, Shelley N.	Minneapolis
‡	Christensen, Llewellyn E.	Minneapolis
	Christenson, Leland R.	Maple Plain
	Clark, Malcolm D.	Minneapolis
‡	Clark, Robert S.	Minneapolis
‡	Clay, Lyman B.	Minneapolis
	Cochrane, Ray F.	Minneapolis
	Coe, John I.	Minneapolis
‡	Cohen, Bernard A.	Minneapolis
	Cohen, Ephraim B.	Minneapolis
	Cohen, Henry W.	Wayzata
‡	Cohen, Sumner S.	Minneapolis
‡	Cole, James S.	Minneapolis
‡	Conlin F. Dixon	Minneapolis
	Conlon, Daniel C.	Minneapolis
‡	Cooper, John P.	Minneapolis
‡	Cooper, Robert R.	Minneapolis
†	Corniea, Albert D.	Minneapolis
‡	Correa, Dale H.	Minneapolis
	Coulter, Harold E.	Minneapolis
	Cowan, Donald W.	Minneapolis
	Craig, M. Elizabeth	Minneapolis
†‡	Cranmer, Richard R.	Minneapolis
	Cranston, Robert W.	Minneapolis
‡	Creevy, Charles D.	Minneapolis
‡	Crowley, Leonard V.	Minneapolis
	Cullado, Andrionico F.	Minneapolis
‡	Culligan, Leo C.	Minneapolis
‡	Cundy, Donald T.	Minneapolis
†	Cushing, Richard T.	Ann Arbor, Michigan
†	Cutts, George	Minneapolis
‡	Daggett, Donald R.	Minneapolis
†‡	Dahl, Elmer O.	Minneapolis
	Dahl, James C.	Minneapolis
†‡	Dahl, John A.	Minneapolis
†	Daniel, Donald H.	Minneapolis
‡	Danyluk, Michael	Minneapolis
	Dargay, Cyril P.	Minneapolis
‡	David, Reuben	Hopkins
	Davis, Eunice A.	Bismarck, N. D.
†‡	Davis, Jay C.	Deerfield Beach, Fla.
	Davis, Michael W.	Minneapolis
	Dawson, Walter J., Jr.	Minneapolis
	Dedeker, Kenneth L.	Minneapolis
*	del Plaine, Carlos W.	Minneapolis
‡	Devereaux, Thomas J.	Wayzata
	Dickman, Roy W.	Minneapolis
‡	Diefenbach, Eugene J.	Minneapolis
	Diehl, Harold S.	New York, New York
‡	Dierker, Heinrich A.	Minneapolis
†	Diessner, Henry D.	Minneapolis
‡	Doan, Robert E.	Wayzata
	Docherty, John A.	Anoka
‡	Donatelle, Edward P.	Minneapolis
†	Dorge, Richard	Minneapolis
	Dornbach, Robert A.	Minneapolis
‡	Dorsey, George C., Jr.	Minneapolis
‡	Dorsey, William E.	Minneapolis
	Doscherholmen, Alfred	Minneapolis
‡	Downing, Wendell K.	Minneapolis
†	Doxey, Gilbert L.	Minneapolis
*‡	Doyle, Lawrence O.	Minneapolis
‡	Dredge, Thomas E., Sr.	Minneapolis
‡	Dredge, Thomas E., Jr.	Minneapolis
	Drill, Frederick E.	Minneapolis
‡	Drill, Herman E.	Hopkins
‡	Duff, Edwin R.	Minneapolis
‡	Dummer, Donald J.	New Brighton
	Duncan, Donald A.	Minneapolis
‡	Dunlap, Earl H.	Minneapolis
‡	Dupont, Joseph A.	Excelsior
	Duryea, Marbry	Minneapolis
‡	Duryea, Willis M.	Minneapolis
‡	Duryea, Willis M., Jr.	Minneapolis
‡	Dvorak, Benjamin A.	Minneapolis
‡	Dwan, Paul F.	Minneapolis
‡	Dworsky, Samuel D.	Minneapolis
‡	Eder, Walter P.	Minneapolis
	Edmondson, Hugh A., Jr.	Minneapolis
‡	Efteland, Myles E.	Minneapolis
†‡	Ehrenberg, Claude J.	Minneapolis
‡	Ehrlich, S. Paul	Minneapolis
	Eich, Matthew A.	Minneapolis
	Eichenlaub, John E.	Minneapolis
‡	Eichhorn, Edmund P., Jr.	Minneapolis
	Eisenstadt, David H.	Minneapolis
‡	Eisenstadt, William S.	Minneapolis
	Eitel, George D.	Minneapolis
†	Ekdale, Robert A.	Palo Alto, Calif.
	Eli, Earl W.	Minneapolis
‡	Ellingson, Richard B.	Minneapolis
*†‡	Ellison, David E.	Minneapolis
‡	Ellison, Evan S.	Minneapolis
	Ellwood, Paul M., Jr.	Minneapolis
	Emond, Albert J.	Farmington
	Emond, Joseph S.	Farmington
‡	Engel, Joseph P.	Minneapolis
‡	Engelhart, Peter C.	Minneapolis
‡	England, Elvin F.	Minneapolis
‡	Engstrand, Oscar J.	Minneapolis
‡	Engstrom, E. Duane	Minneapolis
‡	Erickson, Clifford O.	Minneapolis
‡	Erickson, Laurence F.	Minneapolis
‡	Erickson, Myron E.	Minneapolis
‡	Erickson, Reuben F.	Minneapolis
‡	Esensten, Sidney	Minneapolis
	Espelien, Alan D.	Minneapolis
	Ettinger, Milton G.	Minneapolis
	Etzwiler, Donnell D.	Minneapolis
‡	Evans, Edward T.	Minneapolis
†	Fahr, George E.	Minneapolis
‡	Farber, Lawrence A.	Minneapolis
	Farley, Harrison H.	Minneapolis
‡	Feeney, John M.	Minneapolis
‡	Feigal, David W.	Wayzata
	Feinberg, Philip	Minneapolis
	Feinberg, Samuel B.	Minneapolis
‡	Feinstein, Julius Y.	Minneapolis
‡	Fenger, Ejvind P. K.	Minneapolis
	Fetzek, Albert D.	Minneapolis
‡	Field, Charles W.	Minneapolis
	Fifer, Ellen Z.	Minneapolis
	Fifer, William R.	Minneapolis
	Filiatrault, L. J.	Coon Rapids
‡	Filipovich, Orest N.	Minneapolis
‡	Fingerman, David L.	Minneapolis
‡	Fink, Leo W.	Minneapolis
‡	Fink, Robert J.	Minneapolis
‡	Fink, Walter H.	Minneapolis
	Finley, Paul R.	Minneapolis
	Fisher, Don H.	Minneapolis

Hennepin County Medical Society (Continued)

	Fisher, Isadore	Minneapolis
†	Fjeldstad, C. Alford	Minneapolis
‡	Fleming, Dean S.	Minneapolis
‡	Fliehr, Richard R.	Minneapolis
	Flora, George C.	Minneapolis
‡	Florence, David W.	Robbinsdale
	Foker, Leslie W.	Minneapolis
	Foley, Robert R.	Minneapolis
‡	Folsom, Louis B.	Minneapolis
‡	Forbes, Edward F.	Minneapolis
‡	Ford, W. Harold	Minneapolis
‡	Foster, Orley W.	Minneapolis
†	Fowler, L. Haynes	Newport Beach, Calif.
‡	Fox, James Rogers	Minneapolis
‡	Frane, Donald B.	Minneapolis
‡	Fredericks, George M.	Minneapolis
‡	Freeman, Craig W.	Minneapolis
	Freeman, Donald W.	St. Louis Park
‡	French, Lyle A.	Minneapolis
‡	Frey, Richard J.	Minneapolis
	Friberg, Joseph B.	Minneapolis
‡	Fried, Louis A.	Minneapolis
†‡	Friedell, Aaron	Minneapolis
	Friedell, George	Minneapolis
‡	Friedman, Harry S.	Minneapolis
‡	Friend, Charles A.	Minneapolis
‡	Frost, John B.	Minneapolis
	Frost, Russell H.	Minneapolis
	Fruchtman, Stanley A.	Minneapolis
‡	Frykman, Howard M.	Minneapolis
	Frys, Russell N.	Minneapolis
‡	Fulks, Raymond W.	Minneapolis
†	Fuller, Alice H.	Minneapolis
‡	Funk, Victor K.	Hopkins
	Furman, Christine	Minneapolis
‡	Fusaro, Ramon M.	Minneapolis
‡	Gaard, Richard C.	Minneapolis
	Galbraith, Richard F.	Minneapolis
	Galejs, Aina	Minneapolis
‡	Gallett, Lester	Minneapolis
†	Galligan, Margaret Mary D.	Minneapolis
‡	Gammell, John H.	Minneapolis
‡	Garamella, Joseph J.	Minneapolis
	Garetz, Floyd K.	Minneapolis
‡	Garske, George L.	Minneapolis
	Garten, Joseph L.	Minneapolis
‡	Garvey, James T.	Minneapolis
	Gault, Neal L., Jr.	Minneapolis
†	Gault, Sarah Jane	Minneapolis
‡	Gaviser, David	Minneapolis
‡	Geller, Joseph	Minneapolis
‡	George, Vane P., Jr.	LeSueur
‡	Gibbs, Robert W.	Minneapolis
‡	Giebenhain, John N.	Minneapolis
‡	Giere, Joseph C.	Minneapolis
	Giere, Richard W.	Minneapolis
	Gilbert, Maurice G.	Minneapolis
	Gilbertsen, A. Sigrid	Minneapolis
	Gilbertsen, Victor A.	Minneapolis
	Gingold, Benjamin A.	Minneapolis
‡	Glaeser, John H.	Minneapolis
‡	Godfrey, H. Wilson	Minneapolis
	Gokcan, Muharrem	Minneapolis
‡	Gold, David	Minneapolis
‡	Goldberg, Isadore M.	Minneapolis
	Goldberg, Marvin E.	Minneapolis
‡	Goldberg, Stanley M.	Minneapolis
	Goldfarb, Benjie L.	Minneapolis
	Goldman, Leonard W.	Minneapolis
‡	Goldman, Theodore I.	Minneapolis
‡	Goldner, Meyer Z.	Minneapolis
	Goldstein, Alan L.	Hopkins
‡	Goltz, Robert W.	Minneapolis
‡	Good, Gary	Minneapolis
	Goodchild, William R.	Minneapolis
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	Gordon, Philip E.	Minneapolis
‡	Gordon, Sewell S.	St. Louis Park
‡	Granquist, Richard D.	Minneapolis
	Grant, Suzanne	Minneapolis
†	Gratzek, Frank R.	Anoka
	Gray, Royal C.	Minneapolis
	Green, Clayton R.	Excelsior
	Green, Robert A.	St. Louis Park
‡	Greenberg, Albert J.	Minneapolis
	Greene, Leonard H.	Minneapolis
‡	Greenfield, Irving	Minneapolis
†	Greisheimer, Esther	Philadelphia, Pa.
	Grimes, Marian	Minneapolis
‡	Grimmell, Francis J.	Minneapolis
‡	Grismer, Jerome T.	Minneapolis
	Gronvall, Paul R.	Minneapolis
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	Gruys, Robert I.	Wells
‡	Gullickson, Glenn, Jr.	Minneapolis
‡	Gunlaugson, Frederick G.	Minneapolis
‡	Gustafson, Paul O.	Minneapolis
‡	Gustason, Harold T.	Minneapolis
	Gustilo, Ramon B.	Minneapolis
	Haberer, Helen R.	Minneapolis
‡	Haberle, Charles A.	Minneapolis
‡	Hagen, Kristofer	Minneapolis
‡	Hagen, Wayne S.	Minneapolis
	Haglin, John J.	Minneapolis
‡	Hall, Harry B.	Minneapolis
‡	Hall, Wendell H.	Minneapolis
	Hallin, Roger P.	Minneapolis
‡	Hambidge, Gove, Jr.	Minneapolis
‡	Hamel, Arnold L.	Minneapolis
‡	Hamel, Joseph I.	Minneapolis
	Hammerstrom, Robert N.	Minneapolis
	Handler, Seymour	Minneapolis
‡	Hannah, Hewitt B.	Minneapolis
‡	Hansen, Cyrus O.	Minneapolis
†‡	Hansen, Erling W.	Hopkins
†	Hansen, Olga S.	Minneapolis
‡	Hansen, Rollin M.	Minneapolis
‡	Hanske, Edward A.	Minneapolis
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	Hanson, Harold B.	Minneapolis
	Hanson, Harold W.	Minneapolis
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	Hanson, Mark C. L.	Minneapolis
	Hanson, Mildred S.	Minneapolis
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‡	Hanson, William B.	Minneapolis
‡	Happe, Lawrence J.	Minneapolis
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‡	Hartig, Paul R.	Minneapolis
	Hartman, Evelyn E.	Minneapolis
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†	Harty, Jerome L.	Minneapolis
‡	Hass, Frederick M.	Minneapolis
‡	Hastings, Donald W.	Minneapolis

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Hennepin County Medical Society (Continued)

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	Haugen, John A.	Minneapolis
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†	Hauser. George W.	Seattle, Washington
‡	Havel, Robert J.	Minneapolis
‡	Haven, Walter K.	Minneapolis
‡	Hawkinson, Raymond P.	Minneapolis
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‡	Hays, Albert T.	Minneapolis
‡	Haywa, E. William	Minneapolis
‡	Head, Douglas P.	Minneapolis
‡	Hebbel, Robert	Minneapolis
‡	Hedrick, William L.	Minneapolis
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	Herbert, Willis L.	Minneapolis
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	Hess, Carroll N.	Minneapolis
	Hiatt, John A.	Minneapolis
	Hickok, David F.	Minneapolis
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‡	Hill, Elmer M.	Minneapolis
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‡	Hoffman, Walter Lees	Minneapolis
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	Hovland, Richard D.	Minneapolis
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	Howard, Solomon E.	Minneapolis
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	Ingalls, Edgar G.	Minneapolis
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	Iverson, Eleanor B.	Minneapolis
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	Jackson, Richard L.	Minneapolis
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	Janecek, James, Jr.	Minneapolis
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	Jensen, Reynold A.	Minneapolis
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	Jerome, Elizabeth B. K.	Minneapolis
	Jeub, Robert P.	Minneapolis
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	Johnson, Gordon E.	Minneapolis
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	Johnson, Norman Paul	St. Paul
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	Johnson Youbert T.	Minneapolis
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‡	Kaplan, J. Jacob	Minneapolis
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‡	Karlen, Markle	Minneapolis
	Kasper, Robert E.	Minneapolis
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	Kelly, Charles F.	Minneapolis
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‡	Kelly, John T.	Minneapolis
	Kennedy, Byrl J.	Minneapolis
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	Kennedy, William R.	Minneapolis
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	Kim, Mark K.	Minneapolis
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‡	Koller, Robert L.	Minneapolis
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	Larson, Roger C.	Minneapolis
	Larson, Wyllis G.	Minneapolis
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	Laymon, Carl W.	Minneapolis
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	Lees, David C.	Minneapolis
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	Leighton, John S.	Minneapolis
	Leinonen, Wendla E.	Anoka
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‡	Lenz, Oa	Minneapolis
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‡	Leonard, Samuel	Minneapolis
	Lerner, A. Ross	Minneapolis
	Leslie, W. Robert	Minneapolis
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	Lienke, Roger I.	Robbindale
	Lillehei, C. Walton	Minneapolis
‡	Lillehei, Richard C.	Minneapolis
‡	Limbeck, Donald A.	Robbinsdale
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‡	Lindberg, Winston R.	Minneapolis
‡	Lindblom, Maurice L.	Minneapolis
	Lindeland, Arthur T.	Minneapolis
‡	Lindemann, Charles E.	Minneapolis
‡	Linderholm, Bruce E.	Minneapolis
‡	Lindgren, Russell C.	Minneapolis
‡	Lindquist, Richard H.	Minneaoplis
‡	Linner, Gunnar	Minneapolis
‡	Linner, John H.	Minneapolis
‡	Linner, Paul W.	Minneapolis
	Lipschultz, Oscar	Minneapolis
	Litman, Abraham B.	Minneapolis
‡	Litman, Thomas	Minneapolis
	Lober, Paul H.	Minneapolis
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‡	Logothetis, John A.	Minneapolis
	Loken, Merle K.	Minneapolis
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†	Lovett, Beatrice R.	Minnetonka
	Lowry, Elizabeth C.	Minneapolis
	Lowry, Jeanette K.	Minneapolis
	Lowry, Paul T.	Minneapolis
	Lowry, Thomas	Minneapolis
	Lueck, Wallace W.	Minneapolis
‡	Lufkin, Nathaniel H.	Minneapolis
	Luh, Edwin F.	St. Paul
	Lund, George W.	Minneapolis
†	Lundberg, Ruth I.	St. Paul
†	Lundblad, Roy A.	Minneapolis
	Lundblad, Stanley W.	Minneapolis
†‡	Lundeberg, Karl R.	Minneapolis
‡	Lundquist, Virgil J. P.	Minneapolis
†	Lynch, Matthew J.	Minneapolis
	Lynch, Michael F.	Minneapolis
‡	Lynn, Walter	Minneapolis
	Lyon, Fred A.	Minneapolis
‡	Lyon, John D.	Hopkins
‡	Lyons, James H.	Ventura, Calif.
	Lyons, Michael W.	Minneapolis
†‡	Lysne, Henry	Minneapolis
‡	Lysne, Myron	Minneapolis
	Lysne, Richard B.	Minneapolis
	Lysyj, Anatol	Minneapolis
‡	Lyzenga, Anton G.	Minneapolis
	McCaffrey, F. John	Minneapolis
‡	McCampbell, Malcolm	Minneapolis
‡	McCannel, Malcolm A.	Minneapolis
‡	McCarthy, Donald	Fort Snelling
‡	McCormick, Donald P.	Minneapolis
†	McDaniel, Orianna	Minneapolis
‡	McFarland, Arthur H.	Minneapolis
‡	McGandy, Robert F.	Minneapolis
†‡	McGeary, George E.	No. Ft. Myers, Florida
‡	McInerny, Maurice W.	Minneapolis
	McKelvey, John L.	Minneapolis
‡	McKenna, James L.	Minneapolis
‡	McKenzie, Charles H.	Minneapolis
†‡	McKinlay, Chauncey A.	Minneapolis
‡	McKinlay, Gordon L.	Minneapolis
†	McKinney, Frank S.	Minneapolis
	McLaughlin, Byron H.	Minneapolis
‡	McMurtrie, William B.	Minneapolis
	McNeil, John J.	Minneapolis
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‡	McPheeters, Herman O.	Minneapolis
†‡	MacDonald, Daniel A.	Minneapolis
‡	MacKinnon, Donald C.	Minneapolis
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‡	Mach, John R.	Minneapolis

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Hennepin County Medical Society (Continued)

	Macheledt, Neil L.	Anoka
‡	Madsen, Donald O.	Minneapolis
‡	Maeder, Edward C.	Minneapolis
	Magraw, Richard M.	Minneapolis
‡	Mahle, James P.	Minneapolis
†‡	Maland, Clarence O.	Minneapolis
‡	Malmquist, Carl P.	Minneapolis
	Mandel, Sheldon L.	Minneapolis
‡	Mankey, James C.	Minneapolis
	Mann, George A.	Minneapolis
	Manoles, Ellias N.	Minneapolis
‡	MarCia, Alfred M.	Minneapolis
‡	Mark, Aaron L.	Minneapolis
	Mark, Merle S.	Minneapolis
‡	Marking, George H.	Minneapolis
	Markland, Colin	Minneapolis
	Markovitz, Jack M.	Minneapolis
	Marte, Egon	Minneapolis
‡	Martin, Frank E.	Minneapolis
‡	Martin, George R.	Minneapolis
	Martinson, Carl J.	Wayzata
	Martinson, Elmer J.	Wayzata
‡	Maslansky, Robert A.	Minneapolis
‡	Massee, Joseph S.	Minneapolis
	Mathison, Robert D.	Minneapolis
	Mattson, Hamlin A. N.	Minneapolis
	Maunder, John B.	Minneapolis
†	Maxeiner, Stanley R.	Minneapolis
‡	Maxeiner, S. R., Jr.	Minneapolis
‡	Mayberg, Donald M.	Minneapolis
	Meany, Thomas J.	Minneapolis
‡	Meeker, Henry C.	Minneapolis
	Meekin, Patrick C.	Minneapolis
‡	Meller, Robert L.	Minneapolis
‡	Mensheha, Nicholas M.	Minneapolis
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‡	Merner, Thomas B.	Minneapolis
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	Messenheimer, Myron G.	Minneapolis
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‡	Meyer, Alvin J.	Minneapolis
†	Meyer, E. Lawrence	Winona
†	Michael, Joseph C.	Minneapolis
‡	Michel, Henry H.	Minneapolis
‡	Michelson, Henry E.	Minneapolis
†	Mickelsen, Emma F.	Minneapolis
	Middlebrook, John E.	Minneapolis
‡	Miller, H. Dawes	Minneapolis
	Miller, Harold E.	Minneapolis
‡	Miller, Hugo E.	Minneapolis
‡	Miller, J. Carleton	Minneapolis
‡	Miller, William P.	Minneapolis
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‡	Minder, John G.	Mound
	Minsky, Armen A.	Minneapolis
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‡	Mitchell, Berton D.	Minneapolis
‡	Mitchell, Edward C.	Mound
‡	Mitchell, Mancel	Minneapolis
‡	Mixer, Harry W.	Minneapolis
‡	Moe, John H.	Minneapolis
	Moe, W. Wyatt	Minneapolis
‡	Moehn, John T.	Minneapolis
	Moen, Johannes K.	Minneapolis
	Mollers, Theodore P.	Ft. Snelling
‡	Monson, Einer M.	Minneapolis
‡	Moore, Irvin H.	Hopkins
	Moorhead, Marie	Minneapolis
‡	Moos, Daniel J.	Minneapolis
‡	Moral, Harvey	Minneapolis
‡	Moran, Leo J.	New Brighton
	Moriarty, James A.	Minneapolis
	Moriarty, Joseph D.	Coon Rapids
‡	Mork, A. Harold	Anoka
‡	Mork, Frank E.	Anoka
‡	Mork, Frank E., Jr.	Minneapolis
	Morrison, Charlotte J.	Minneapolis
‡	Mosser, Donn G.	Minneapolis
‡	Moyer, Leonard B.	Minneapolis
‡	Mulholland, William	Minneapolis
	Mullin, Gerald T.	Minneapolis
	Mulvahill, John E.	Minneapolis
	Munkittrick, Ronald C.	Minneapolis
‡	Murphy, Edmund P.	Minneapolis
	Murray, Elisabeth M.	Minneapolis
	Muske, Marvin M.	Minneapolis
‡	Musty, Nicholas J.	Minneapolis
‡	Myers, Jay A.	Minneapolis
‡	Myhre, James	Minneapolis
‡	Nagobads, Ilgvars J.	Minneapolis
	Nagobads, V. George	So. St. Paul
	Nash, Eldore B.	Minneapolis
‡	Naslund, Ames W.	Minneapolis
	Nauth, Bernard S.	Minneapolis
†‡	Neal, Joe M.	Minneapolis
‡	Neary, Richard P.	Minneapolis
†	Nelson, Bernette G.	Slayton
†	Nelson, Bernice A.	Minneapolis
	Nelson, C. Barton	Minneapolis
	Nelson, Carleton	Minneapolis
‡	Nelson, David J.	Minneapolis
‡	Nelson, Edward N.	Minneapolis
‡	Nelson, George E.	Minneapolis
	Nelson, Gunard A.	Minneapolis
‡	Nelson, Harvey	Minneapolis
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	Nelson, Maxine O.	Minneapolis
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	Neumann, Roland F.	Minneapolis
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	Nielsen, David J.	Minneapolis
	Nolan, Robert K.	Minneapolis
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‡	Noran, Harold H.	Minneapolis
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†	Nordin, Gustaf T.	Honolulu, Hawaii
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‡	Nordland, Martin A.	Minneapolis
	Norman, Franklin C.	Minneapolis
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	Norval, Mildred A.	St. Paul
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	O'Brien, Bruce J.	Minneapolis
‡	O'Brien, William A.	Minneapolis
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	Olavs, Olga	Minneapolis
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	Olson, Robert W.	Minneapolis
	Olson, Rolland A.	Wayzata
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‡	Oppen, E. Gerhard	Minneapolis
‡	Oppen, Melvin G.	Minnetonka
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	Owen, Richard R.	Minneapolis
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	Page, Raymond L.	Minneapolis
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	Papermaster, Ralph	Minneapolis
	Papermaster, Theodore C.	Minneapolis
	Park, Wilford E.	Minneapolis
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	Paule, William J.	Minneapolis
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	Peper, Martin C.	Minneapolis
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	Perlman, Herschel L.	Minneapolis
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	Peterson, John A.	Minneapolis
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†‡	Petit, Leon J.	Minneapolis
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‡	Proshek, Lumir C.	Minneapolis
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‡	Quist, Henry W., Jr.	Minneapolis
	Raab, David E.	Minneapolis
	Racer, Harley J.	Minneapolis
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	Randall, David A.	Minneapolis
‡	Ransom, H. Robert	Osseo
‡	Ratelle, Alexander E.	Minneapolis
	Recht, Thomas M.	Minneapolis
	Reed, Sheldon C.	Minneapolis
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‡	Regnier, Edward A.	Minneapolis
	Reichel, Samuel M.	Minneapolis
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‡	Reiser, Milton P.	Minneapolis
‡	Remole, William D.	Minneapolis
‡	Resch, Joseph A.	Minneapolis
‡	Reynolds, Donald P.	Minneapolis
	Rholl, Arnold O.	Minneapolis
‡	Rice, Carl O.	Minneapolis
	Rice, Fred A.	Minneapolis
‡	Richardson, Robert J.	Minneapolis
†‡	Richdorf, Lawrence F.	Minneapolis
‡	Rieke, Wellington W.	Wayzata
	Riordan, Elsie M.	Minneapolis
	Ripple, Rudolph J., Jr.	Minneapolis
‡	Risch, Ronald E.	Minneapolis
‡	Rizer, Dean K.	Minneapolis
†	Robb, Edwin F.	Boca Raton, Florida
‡	Robbins, Owen F.	Minneapolis
‡	Roberts, Byron H.	Minneapolis
	Roberts, Lewis J.	Minneapolis
‡	Roberts, Stanley W.	Minneapolis
	Robinson, Cortland O.	Minneapolis
‡	Rock, William H.	Anoka
‡	Rocknem, Robert E.	Minneapolis
	Rockwell, Curtiss V.	Minneapolis
‡	Rodgers, Richard S.	Minneapolis
‡	Rogin, Norton	Minneapolis
‡	Rollins, Pat	Minnetonka
‡	Romness, Kenneth B.	Mound
‡	Rosenbaum, David L.	Minneapolis
‡	Rosendahl, Frederick G.	Minneapolis
‡	Rosenfield, Abraham B.	Minneapolis
‡	Rosenow, John H.	Minneapolis
†	Rosenwald, Reuben M.	Robbinsdale
‡	Rossen, Ralph	Minneapolis
	Rotenberg, Robert J.	Minneapolis
	Rotenberg, Samuel	Huntington Park, Calif.
‡	Rothnem, Morris S.	Minneapolis
	Rucker, Thomas K.	Minneapolis
	Rucker, William H.	Minneapolis
†	Rud, Norman E.	Minneapolis
	Runquist, Richard K.	Cambridge
‡	Russeth, Arthur N.	Minneapolis
‡	Rusten, Elmer M.	Minneapolis
	Rydberg, John S.	Minneapolis
	Rydburg, Wayne C.	Minneapolis

Continued on Next Page

Hennepin County Medical Society (Continued)

‡	Rydland, Arne D.	Minneapolis
‡	St. Cyr, Harry M.	Robbinsdale
‡	St. Cyr, Kenneth J.	Minneapolis
	Salchert, John	Minneapolis
‡	Saliterman, Bernard I.	Minneapolis
‡	Salovich, Edward L.	Minneapolis
	Salovich, Elmer R.	Minneapolis
‡	Sandt, Karl E.	Minneapolis
‡	Sanfilippo, Sylvester J.	Minneapolis
	Sartor, Richard	Minneapolis
‡	Sborov, Abe M.	Minneapolis
	Scallen, Raymond W.	Minneapolis
	Schaar, Frances E.	Minneapolis
	Schaefer, Wesley G.	Minneapolis
	Schaffhausen, Irwin F.	Minneapolis
	Schaffhausen, Mildred	Minneapolis
†	Scheldrup, N. H.	Minneapolis
‡	Scherer, L. Raymond	Minneapolis
	Scherling, Sidney S.	Minneapolis
	Schiele, Burtrum C.	Minneapolis
‡	Schissel, Gregory A.	Minneapolis
‡	Schmidt, W. Robert	Minneapolis
†	Schmitt, S. C.	Fallbrook, California
	Schneck, Jack I.	Minneapolis
‡	Schoening, Herbert A.	Minneapolis
‡	Schottler, Max E.	Minneapolis
‡	Schrader, Wayne H.	Minneapolis
‡	Schroeder, Albert J.	Minneapolis
‡	Schultz, Alvin L.	Minneapolis
	Schultz, Earl A.	Minneapolis
‡	Schultz, J. Harold	Minneapolis
‡	Schultz, Peter J.	Minneapolis
‡	Schulze, William M.	Minneapolis
‡	Schumacher, John W.	Minneapolis
‡	Schwartz, E. Robert	Minneapolis
†‡	Schwartz, Virgil J.	Minneapolis
‡	Scott, Horace G.	Minneapolis
†	Seaberg, John A.	Pequot Lakes
‡	Seay, James E., III	Minneapolis
	Segal, Edward L.	Minneapolis
‡	Segal, Martin A.	Minneapolis
†	Seham, Max	St. Paul
	Seibel, David I.	Minneapolis
	Seifert, Gregory L.	Excelsior
‡	Seifert, Milton H.	Excelsior
‡	Seifert, Milton H., Jr.	Excelsior
	Semba, Thomas	Minneapolis
‡	Semsch, Robert D.	Wayzata
	Severseike, Odean M.	Minneapolis
‡	Shandorf, James F.	Minneapolis
	Shaperman, Eva P.	Minneapolis
‡	Shapiro, Irving	Minneapolis
‡	Shapiro, Sidney K.	Minneapolis
	Shapiro, Stanley W.	Minneapolis
	Sharp, David	Berkeley, Calif.
‡	Shattuck, Clark A.	Minneapolis
‡	Shaw, Howard A.	Minneapolis
‡	Shea, Andrew W	Minneapolis
‡	Sher, Lewis	Minneapolis
‡	Sherman, Lloyd F:	Minneapolis
‡	Sherman, Morris H.	Minneapolis
†	Shillington, Maurice A.	Fort Lauderdale, Florida
	Sholler, Lawrence J.	Minneapolis
‡	Shragg, Robert I.	Minneapolis
‡	Shronts, John F.	Minneapolis
‡	Sidell, Franklin D.	Minneapolis
	Siegmann, William C.	Minneapolis
	Sigel, Melvin E.	Minneapolis
‡	Silas, Ralph M.	Minneapolis
	Silver, John D.	Minneapolis
‡	Simmons, Richard K.	Minneapolis
†	Simons, Jalmar H.	Minneapolis
‡	Simonson, Donald B.	Minneapolis
†	Simpson, Ellery De W.	Phoenix, Arizona
	Sinning, John E., Jr.	Minneapolis
‡	Sinykin, Melvin B.	Minneapolis
‡	Sipe, James W.	Coon Rapids
*	Siperstein, David M.	Minneapolis
‡	Skjold, Arthur C.	Minneapolis
	Smiley, John T.	Minneapolis
‡	Smisek, Frank M.	Minneapolis
†	Smith, Adam M.	Minneapolis
‡	Smith, Archie M.	Minneapolis
‡	Smith, Baxter A., Jr.	Minneapolis
‡	Smith, Graham G.	Minneapolis
‡	Smith, John E.	Minneapolis
†	Smith, Margaret I.	Gardena, California
	Smith, Nadine G.	Minneapolis
	Smith, Norvin R.	Hastings
‡	Smith, Theodore S.	Minneapolis
‡	Soderlind, Ragnar T.	Minneapolis
‡	Solhaug, Samuel B.	Minneapolis
‡	Solvason, Harold M.	Minneapolis
	Spain, W. Thomas	Evansville, Indiana
‡	Spano, Joseph P.	Minneapolis
‡	Spencer, Bernard J.	Minneapolis
‡	Spencer, David L.	Anoka
‡	Spink, Wesley W.	Minneapolis
‡	Sponsel, Kenath H.	Minneapolis
†	Spratt, Charles N.	Phoenix, Arizona
‡	Stahr, Aubrey C.	Hopkins
†	Stanford, Charles E.	Elcho, Wisconsin
†	Stanley, Court R.	Minneapolis
‡	Staub, Henry P.	Minneapolis
	Steidl, Richard M.	Minneapolis
	Steiner, Andrew M.	Minneapolis
‡	Stelter, Lloyd A.	Minneapolis
*‡	Stennes, John L.	Minneapolis
†	Stenstrom, Annette T.	Anna Maria, Florida
	Stenzel, Joseph A.	Minneapolis
‡	Stephens, William E.	Minneapolis
	Sterrie, Norman A.	Minneapolis
‡	Stewart, Marvin J.	Minneapolis
‡	Stiegler, Farrell S.	Minneapolis
‡	Stoesser, Albert V.	Minneapolis
#	Stolee, Curtis N.	W. Dauphin, Madagascar
†	Stolee, Thomas A.	Minneapolis
‡	Stoltz, Robert C.	Minneapolis
	Stone, Norman F.	Minneapolis
	Stone, Stanley P.	Minneapolis
‡	Story, Jim L.	Minneapolis
‡	Strait, Herbert S.	Minneapolis
‡	Streu, Richard E.	Minneapolis
‡	Strickler, Jacob H.	Minneapolis
‡	Strom, Gordon W.	Minneapolis
‡	Strom, Robert L.	Minneapolis
‡	Stromgren, Delph T.	Minneapolis
‡	Stromme, William B.	Minneapolis
	Strunk, Clarence A.	Minneapolis
	Student, Richard E.	Minneapolis
‡	Sturges, Robert L	Minneapolis
	Subak, Barbara H.	Minneapolis
‡	Subby, Walter	Wayzata
	Sukov, Marvin	Minneapolis
‡	Swanson, David A.	Minneapolis
‡	Sweetser, Horatio B.	Minneapolis
‡	Sweetser, Theodore H.	Minneapolis

Hennepin County Medical Society (Continued)

‡	Sweetser, Theodore H., Jr.	Minneapolis
†‡	Swendseen, Carl G.	Minneapolis
‡	Swendseen, Carl J.	Minneapolis
	Swenson, Floyd J.	Minneapolis
	Swenson, Richard W.	Minneapolis
	Symchych, Boris E.	Minneapolis
‡	Tam, Ernest C.	Minneapolis
	Tambornino, Joseph M.	Minneapolis
‡	Tanaka, Shin	Minneapolis
†‡	Tangen, George M.	Taylor Falls
	Tangen, George V.	Minneapolis
†	Taylor, Joseph H.	Ft. Lauderdale, Fla.
‡	Taylor, William E.	Minneapolis
	Tenczar, Francis J., Jr.	Chicago, Ill.
‡	Tenner, Robert J.	Minneapolis
‡	Teska, Byron A.	Minneapolis
‡	Teynor, Joseph W.	Minneapolis
	Thelemann, Arthur R., Jr.	Minneapolis
	Theobalt, Inge M.	Minneapolis
‡	Thomas, William H.	Long Lake
	Thomes, A. Boyd	Minneapolis
	Thompson, Arthur	Minneapolis
†‡	Thompson, Willis H.	Minneapolis
	Thorsen, David S.	Minneapolis
‡	Thorson, Stuart V.	Minneapolis
‡	Thysell, Desmond M.	Minneapolis
‡	Titrud, Leonard A.	Minneapolis
	Tobin, John D.	Minneapolis
	Torres, Fernando	Minneapolis
	Trach, Benedict B.	Minneapolis
‡	Trost, Francis J.	Minneapolis
‡	Trow, James E.	Minneapolis
	Trow, William H.	Hopkins
	Trucker, Earl B.	Minneapolis
	Tsai, Shih Hao	Minneapolis
‡	Tucker, Richard C.	Minneapolis
‡	Tudor, Richard B.	Minneapolis
*†	Turnacliff, Dale D.	St. Paul
‡	Twidwell, Joseph E.	Minneapolis
	Twomey, John E.	Minneapolis
‡	Ulvestad, Harold S.	Minneapolis
‡	Utendorfer, Robert W.	Minneapolis
	Vaaler, Robert T.	Minneapolis
‡	Valgemae, Romil	Minneapolis
	Veinbergs, Arnolds	Minneapolis
‡	Vellek, Donald G.	Minneapolis
	Vennes, Jack A.	Minneapolis
	Vik, A. Elliott	Minneapolis
‡	Von Drashek, Stanley C.	Minneapolis
	Vroman, Donald C.	Minneapolis
	Wagner, Christian	Minneapolis
‡	Wagner, Robert M.	Minneapolis
‡	Wahlquist, Harold F.	Minneapolis
†	Waldron, Carl W.	Scottsdale, Arizona
	Waldron, John F.	Minneapolis
‡	Wall, Carl R.	Minneapolis
	Wallinga, Jack V.	Minneapolis
‡	Walonick, Albert L.	Minneapolis
	Walsh, Francis M.	Minneapolis
	Walsh, William T.	Minneapolis
	Wang, Yang	Minneapolis
‡	Wangensteen, Owen H.	Minneapolis
	Warren, John W.	Minneapolis
	Waters, Alvin W.	St. Paul
‡	Watson, C. Gordon	Minneapolis
	Watson, Cecil J.	Minneapolis
	Wattenberg, Lee W.	Minneapolis
	Weatherhead, Donald S. P.	Minneapolis
‡	Webb, Edgar A.	Minneapolis
‡	Webber, Richard J.	St. Louis Park
‡	Weber, Lowell W.	Minneapolis
‡	Weisberg, Rapheal J.	Minneapolis
‡	Weiss, Leo	Minneapolis
‡	Wendland, John P.	Minneapolis
	Werner, George	Minneapolis
‡	Wesolowski, Stanley	Minneapolis
†	West, Catherine C.	Edina
‡	Westgate, Hugh D.	Minneapolis
	Wetherby, Macnider	Minneapolis
	Wetherby, Macnider, Jr.	Minneapolis
	Wethington, Joseph F.	Coon Rapids
‡	Wett, Richard J.	Minneapolis
	Wexler, Harold M.	Minneapolis
‡	Wheeler, Robert W.	Minneapolis
	Whitacre, John C., II	Norman, Okla.
	White, Asher A.	Minneapolis
†	White, S. Marx	Minneapolis
†	White, Willard D.	Minneapolis
‡	Whitesell, Lloyd A.	Minneapolis
‡	Widen, Wilford F.	Minneapolis
	Wigg, Norman P.	Minneapolis
‡	Wilcox, William A.	Minneapolis
	Wild, John J.	Minneapolis
†	Wilder, Kenneth W.	Minneapolis
†	Wilder, Robert L.	Minneapolis
†	Wilder, Russell M., Jr.	Topeka, Kansas
‡	Wilder, Walter L.	Minneapolis
‡	Wilken, Paul A.	Minneapolis
	Williams, Henry L.	Minneapolis
	Williams, Paul A.	Minneapolis
‡	Williams, Richard E.	Robbinsdale
	Willis, Harper F., Jr.	Minneapolis
‡	Wilson, Robert E.	Minneapolis
	Wilson, Thomas M., Jr.	Minneapolis
	Winchell, Paul	Minneapolis
†	Winther, Nora M. C.	Columbus, Ohio
‡	Wippermann, Frederic F.	Minneapolis
‡	Wisiol, Erich S.	Minneapolis
	Wisness, Osmund A.	Minneapolis
*†	Witham, Carl A.	Minneapolis
*†‡	Wittich, Frederick W.	Minneapolis
	Woellner, Richard C.	Minneapolis
†‡	Wohlrabe, Arthur A.	Minneapolis
‡	Wohlrabe, A. Cabot	Minneapolis
‡	Wohlrabe, Robert G.	Minneapolis
‡	Wolf, Alfred H.	Minneapolis
‡	Wolter, Frederick H.	Minneapolis
	Woodley, Donald W.	Minneapolis
	Worrell, Philip J.	Minneapolis
‡	Woyda, William C.	Minneapolis
	Wright, Donald L.	Minneapolis
‡	Wright, Thomas D.	Minneapolis
*‡	Wright, Wale S.	Minneapolis
‡	Wright, William S.	Edina
‡	Wuest, Frederick C.	Minneapolis
†	Wynne, Herbert M. N.	Minneapolis
	Yeager, Terrell F.	Anoka
‡	Yelle, Matthew D.	Anoka
‡	Ylvisaker, Ragnvald S.	Minneapolis
*†‡	Yoerg, Otto W.	Minneapolis
	Yonehiro, Earl G.	Minneapolis
	Yue, Wen Y.	Excelsior
	Zahrendt, O. Lewis	Minneapolis
‡	Zarling, V. Richard	Minneapolis
‡	Zaworski, Leo A.	Minneapolis
	Zelickson, Alvin S.	Minneapolis
	Zierold, Arthur A.	Minneapolis
‡	Zinn, Charles W.	Wayzata
‡	Zinter, Ferdinand A.	Minneapolis

KANDIYOHI-SWIFT-MEEKER COUNTY MEDICAL SOCIETY

Kandiyohi, Swift and Meeker Counties
Regular meetings Third Thursday of each month
Annual meeting in November
Number of members 51

PRESIDENT		
	Johnson, Marvin W.	Dassel
SECRETARY		
	Hinz, Walter E.	Willmar
‡	Allison, David D.	Litchfield
†	Anderson, Richard E.	Willmar
‡	Bosland, Howard G.	Willmar
‡	Carlson, Robert G.	Willmar
	Chunn, Stanley S.	Willmar
	Danielson, Lennox	Litchfield
‡	Dille, Donald E.	Litchfield
‡	Docksey, John W.	Willmar
‡	Dunstan, Paul L.	Willmar
	Eberley, Tobe S.	Benson
‡	Ellinger, Albert J.	Willmar
†	Fedor, Robert D.	South St. Paul
†	Frederickson, Alice C.	Willmar
	Gaebe, Milton B.	Clara City
†	Giere, Silas W.	Crookston
‡	Gilman, Lloyd C.	Willmar
	Griffin, Richard P.	Benson
‡	Guy, Jack A.	New London
‡	Hinderaker, Harris P.	Willmar
‡	Hinz, Walter E.	Willmar
‡	Hodapp, Robert V.	Willmar
	Houts, Joseph C.	Dassel
	Jacobs, Douglas L.	Willmar
‡	Johnson, Marvin W.	Dassel
‡	Kaufman, Edward J.	Appleton
	McCarthy, Austin M.	Willmar
	Macklin, William E.	Litchfield
‡	Meinert, John K.	Willmar
‡	Michels, Roger P.	Willmar
‡	Munneke, Lyle	Clara City
‡	Nelson, Robert H.	Benson
	Nolen, William A.	Litchfield
‡	Olson, Gregory M.	Litchfield
‡	Opsahl, Lawrence	Willmar
	Petersen, Donald H.	Willmar
‡	Peterson, Willard E.	Willmar
†	Porter, Oliver M.	Minneapolis
‡	Proeschel, Ray K.	Willmar
‡	Robinson, William W.	New London
‡	Rorem, Joseph A.	Appleton
‡	Ruchie, Warren H.	Willmar
‡	Ruhe, Albert	Willmar
	Rygh, Harold N.	Atwater
	Schnell, Frederick S.	Litchfield
	Skaife, William F.	Benson
	Smith, Lloyd A.	Willmar
†‡	Solsem, Frederick N. S.	Spicer
‡	Thompson, Russell A.	Willmar
‡	Wagner, Norman W.	Benson
	Wilmot, Cecil A.	Litchfield
	Wilmot, Harold E.	Litchfield

LYON-LINCOLN COUNTY MEDICAL SOCIETY

Lyon and Lincoln Counties
Regular meetings, 6 meetings Spring and Fall
Annual meeting fourth Tuesday in October
Number of members 27

PRESIDENT		
	Mueller, LeRoy	Hendricks
SECRETARY		
	Boyum, Allan J.	Marshall
‡	Bodaski, Albert A.	Tyler
‡	Boyum, Alan J.	Marshall
‡	Eckdale, John E.	Marshall
†	Engwall, Richard L.	Minneapolis
‡	Ferguson, William C.	Walnut Grove
‡	Ford, Burton C.	Marshall
‡	Hedenstrom, Philip C.	Marshall
*†	Hermanson, Peter E.	Hendricks
†	Hoidale, Andrew D.	Tracy
‡	Johnson, C. Percy	Tyler
†	Kreuzer, Titus C.	Fort Snelling
‡	Lee, Norman J.	Tracy
‡	Monson, Leonard J.	Canby
‡	Mueller, LeRoy E.	Hendricks
‡	Muesing, Mark A.	Tyler
‡	Murphy, Joseph E.	Marshall
‡	Myers, John W.	Canby
‡	Olson, Robert T.	Canby
‡	Peterson, Kenneth A.	Marshall
‡	Remsberg, Robert R.	Tracy
†	Rohrer, Christian A.	Madison Lake
‡	Sutherland, John E.	Marshall
‡	Taintor, Ronald W.	Marshall
†	Thill, Leonard J.	Traverse City, Mich.
‡	Thompson, Carl O.	Hendricks
†	Vadheim, Alfred L.	Brookings, South Dakota
†	Workman, Warner G.	Tracy
†	Yaeger, Wilbert W.	Excelsior

MC LEOD COUNTY MEDICAL SOCIETY

McLeod County
Regular meetings, third Thursday of each month
Annual meeting, third Thursday in November
Number of members 22

PRESIDENT		
	Griebie, Grant L.	Brownton
SECRETARY		
	Smyth, John J.	Lester Prairie
	Blackwell, Leonard H.	Glencoe
‡	Bretzke, Carl O.	Hutchinson
	Carroll, John J.	Winsted
‡	Chervenak, William A.	Minneapolis
‡	Dysterheft, Adolf F.	Gaylord
‡	Griebie, Grant L.	Brownton
‡	Huebert, Dan W.	Hutchinson
‡	Jensen, Alvin M.	Brownton
‡	Kapsner, Adrian L.	Hutchinson
	Knoche, Harvey A.	Gaylord
‡	Lippmann, Elmer W.	Hutchinson
‡	McCoy, Donald E.	Glencoe
‡	McNeil, Maurice R.	Glencoe
‡	Navratil, Donald R.	Glencoe
‡	Peterson, Kenneth H.	Hutchinson
‡	Neumaier, Arthur	Glencoe
‡	Schroeppel, John E.	Winthrop
‡	Selmo, Joseph D.	Norwood
‡	Smith, George R.	Hutchinson
‡	Smyth, John J.	Lester Prairie
	Stifter, A. J.	Winsted
‡	Truesdale, Clark W.	Glencoe

MOWER COUNTY MEDICAL SOCIETY

Mower County
Regular meetings, last Friday of the month
Annual meeting, November
Number of members 41

PRESIDENT		
	Lommen, Morris L.	Austin
SECRETARY		
	Todd, John C.	Austin
‡	Anderson, David P., Jr.	Austin
‡	Anderson, Harold J.	Austin
‡	Barber, Tracy E.	Austin
‡	Christian, William L.	Austin
‡	Cronwell, Bernhard J.	Austin
‡	Fisch, Herbert M.	Austin
‡	Hagen, John D.	Austin
†	Havens, John G. W.	Minneapolis
†	Hertel, Garfield E.	McAllen, Texas
‡	Hesla, Inman A.	Austin
‡	Isele, Reginald H.	Austin
†‡	Leck, Paul C.	Austin
‡	Lommen, Morris L.	Austin
†‡	Lommen, Peter A.	Austin
‡	Lommen, Peter A., Jr.	Austin
†	McKenna, Jay K.	LaJolla, California
‡	Mathers, John E.	Austin
‡	Miller, Herman	Austin
‡	Mlinar, Joseph P.	Austin
†	Morse, Morton P.	LeRoy
	Morse, Roger D.	LeRoy
‡	Muchow, Gene C.	Austin
‡	Nesse, James A.	Austin
‡	O'Rourke, William J.	Austin
‡	Osborn, Donald O.	Austin
‡	Patten, John C.	Austin
‡	Peterson, Stanley C.	Austin
‡	Roberts, George A.	Austin
†	Robertson, Paul A.	Austin
‡	Rosenthal, F. Harold	Austin
‡	Seery, Thomas M.	Austin
‡	Sheedy, Chester L.	Austin
†	Smythe, Gwendolyn	Austin
‡	Smythe, Lowell J.	Austin
‡	Stahl, George W.	Austin
‡	Taufic, Mansur	Austin
	Thomson, James M.	Austin
‡	Todd, John C.	Austin
‡	Twiggs, Leo F.	Austin
‡	Van Cleve, Horatio P., Jr.	Austin
‡	Wright, Robert R.	Austin

NICOLLET-LE SUEUR COUNTY MEDICAL SOCIETY

Nicollet and LeSueur Counties
Regular meetings, first Monday of alternate months
Annual meeting, December
Number of members 29

PRESIDENT		
	Olmanson, M. Don	St. Peter
SECRETARY		
	Anderson, Jo E.	LeSueur
‡	Anderson, Jo E.	LeSueur
‡	Bergeron, Dale A.	LeSueur
†	Branham, Donald S.	Deer Park, Wis.
	Brink, Donald	St. Peter
‡	Curtis, Rauen A.	Le Center
‡	Engstrom, George E.	St. Peter
†	Ericson, Swan	Los Angeles, California
	Gislason, Solveig T.	St. Peter
‡	Greene, Gordon	Arlington
‡	Gridley, John W.	St. Peter
‡	Grimes, Burton P.	St. Peter
	Haes, Julius E.	St. Peter
‡	Hiniker, Peter J.	LeSueur
†	Kabrick, Ola A.	Hull, Illinois
	Kath, Reinhard H.	Arlington
	Larson, Milo H.	St. Peter
‡	Lenander, Mellvin E. L.	St. Peter
	Ninneman, Newton N.	St. Peter
‡	Olmanson, Edmund G.	St. Peter
	Olmanson, M. Donald	St. Peter
‡	Olmanson, Vern	St. Peter
	Sauer, Jean C.	St. Peter
	Sheppard, Charles G.	St. Peter
‡	Sjostrom, Lawrence E.	St. Peter
‡	Sonnesyn, Nels N.	LeSueur
‡	Strathern, Carleton S.	St. Peter
	Thompson, A. Henry	St. Peter
‡	Walden, Archie D.	LeSueur
	Wohlrabe, Clarence F.	North Mankato

PARK REGION DISTRICT AND COUNTY MEDICAL SOCIETY

Douglas, Grant, Otter Tail & Wilkin Counties
Regular meetings, March, June, September and December
Annual meeting, December
Number of members 66

	PRESIDENT	
	Campbell, Denis V.	Fergus Falls
	SECRETARY	
	Sethre, Arthur E.	Fergus Falls
†	Arndt, Harry W.	Detroit Lakes
	Baker, Jeannette L.	Fergus Falls
	Baker, Norman H.	Fergus Falls
‡	Bateman, Clarence V.	Fergus Falls
‡	Boline, Clifford A.	Battle Lake
‡	Cain, James H.	Alexandria
‡	Campbell, Denis V.	Fergus Falls
‡	Carlson, Carl E.	Alexandria
	Carlson, Homer J.	Pelican Rapids
‡	Clifford, George W.	Alexandria
‡	Colman, Edward L.	Fergus Falls
‡	Daehlin, Rolf	Fergus Falls
	Doms, Vernon A.	Elbow Lake
‡	Eddy, Richard L.	Alexandria
‡	Emerson, Edwin E.	Osakis
‡	Estrem, Ralph L.	Fergus Falls
‡	Estrem, Robert D.	Fergus Falls
‡	Geiser, Peter M.	Alexandria
‡	Hanson, Everett C.	New York Mills
‡	Heegaard, William G.	Alexandria
‡	Helseth, Hovald K.	Fergus Falls
†	Hildebrand, L. D.	Minneapolis
‡	Hom, Leong Y. W.	Battle Lake
‡	Jacobson, Clifford W.	Breckenridge
‡	Johnson, Arthur G., Jr.	Fergus Falls
‡	Kevern, Jay L.	Henning
‡	Kippen, Neil	Breckenridge
‡	Korda, Henry A.	Pelican Rapids
‡	Kuhlmann, Vernon G.	Alexandria
	Larson, Dorette W.	Fergus Falls
‡	Lewis, Charles W.	Henning

†	Love, Frederick A.	Carlos
	Lu, Cheng-en	Fergus Falls
‡	Lund, Carl J. T.	Fergus Falls
†	Mortensen, Nels G.	Minneapolis
‡	Mouritsen, Glenn J.	Fergus Falls
†‡	Nakamura, James Y.	Excelsior
‡	Nelson Roy A.	Fergus Falls
‡	Ness, Richard A.	Fergus Falls
‡	Nicholson, Richard W.	Fergus Falls
‡	O'Brien, Louis T.	Breckenridge
‡	Orandi, Mehdi	Fergus Falls
	Ostergaard, Erling	Elbow Lake
	Parson, E. Lillian B.	Elbow Lake
†	Parson, Lester R.	Elbow Lake
†	Patterson, William L.	Fergus Falls
	Pawlyszyn, Julian	Fergus Falls
‡	Perkins, Douglass E.	Alexandria
‡	Reinhardt, James H.	Alexandria
‡	Richter, Paul H.	Fergus Falls
‡	Rockwood, Philo H.	Fergus Falls
‡	Sanderson, David J.	Fergus Falls
	Sather, Edgar R.	Alexandria
	Schamber, Walter E.	Parkers Prairie
	Schoeneberger, P. B.	Perham
‡	Sethre, Arthur F.	Fergus Falls
‡	Shaver, Ward	Fergus Falls
	Sporre, Knute A.	Fergus Falls
‡	Stahn, Louis H.	Fergus Falls
‡	Stemsrud, Harold L.	Alexandria
‡	Syverson, Leslie A.	Fergus Falls
‡	Tanquist, Edwin J.	Alexandria
‡	Tanquist, Edwin J., Jr.	Alexandria
	Warner, James J.	Perham
‡	Wasson, Loren F.	Alexandria
‡	Webb, Alexander G.	Elbow Lake

RAMSEY COUNTY MEDICAL SOCIETY

Ramsey County
Regular meetings, last Monday each month except June, July & August
Annual meeting in January
Number of members 548

	PRESIDENT	
	Scott, Eugene E.	St. Paul
	SECRETARY	
	Hollinshead, William H.	St. Paul
	SEC'Y-EXECUTIVE OFFICE	
	Olson, Mrs. Eleanor	St. Paul
‡	Abrams, Alexander, Jr.	St. Paul
‡	Adair, Albert F., Jr.	St. Paul
	Adams, Harold R.	St. Paul
‡	Ahrens, Robert M.	St. Paul
‡	Albrecht, Raymond J.	St. Paul
‡	Alden, John F.	St. Paul
‡	Alton, Donald G.	St. Paul
‡	Amerongen, Werner W.	St. Paul
	Anderson, James J.	St. Paul
	Anderson, Margaret C.	St. Paul

*‡	Arnquist, Andrew S.	St. Paul
‡	Arny, Frederick P.	St. Paul
‡	Arzt, Philip K.	St. Paul
	Ashmore, Herbert C.	St. Paul
‡	Aurelius, J. Richards	St. Paul
‡	Ausman, Duane R.	St. Paul
‡	Austrian, Sol	St. Paul
‡	Babb, Frank S.	St. Paul
	Bach, Jerome M.	St. Paul
	Baker, Chilton R., Jr.	St. Paul
	Balce, Regino V.	St. Paul
*	Balcome, Milton M.	St. Paul
	Barnett, Joseph M.	St. Paul
†	Barsness, Nellie O. N.	St. Paul
	Bauer, Eugene L.	St. Paul

Ramsey County Medical Society (Continued)

‡	Beck, Charles J.	North St. Paul
‡	Beek, Harvey O.	St. Paul
‡	Beer, John J.	St. Paul
‡	Bellomo, James	St. Paul
	Belz, Reinmar	St. Paul
‡	Benepe, James L.	St. Paul
	Benthack, Elaine M.	St. Paul
	Bernier, M. J.	North St. Paul
‡	Bernstein, William C.	St. Paul
‡	Bicek, Joseph F.	St. Paul
‡	Bjornson, Robert G. B.	St. Paul
	Black, Earl J.	St. Paul
	Blackburn, Henry W., Jr.	St. Paul
‡	Blomberg, William R.	St. Paul
‡	Blumberg, Henry B.	St. Paul
†	Bock, Rolland A.	St. Paul
‡	Bonello, Frank J.	St. Paul
‡	Borg, Joseph F.	St. Paul
†	Bouma, Lewis R.	St. Paul
‡	Brainard, John B.	St. Paul
†	Bray, Elwyn R.	St. Paul
‡	Briggs, John F.	St. Paul
‡	Briggs, Thomas G.	White Bear Lake
‡	Broadie, Thomas E.	St. Paul
†‡	Brodie, Walter D.	St. Paul
	Broman, Harold R., Jr.	North St. Paul
	Brown, Hector M.	St. Paul
	Brown, James E., Jr.	St. Paul
†	Brown, John M.	Rochester
‡	Bulinski, Theodore J.	St. Paul
‡	Burklund, Edwin C.	St. Paul
‡	Burlingame, David A.	St. Paul
‡	Burmeister, Richard O.	St. Paul
†	Burns, John M.	St. Paul
*†	Burton, Carl G.	St. Paul
	Burton, J. Richard	St. Paul
‡	Bush, Robert P.	St. Paul
†‡	Busher, Herbert H.	St. Paul
‡	Byrne, William J.	St. Paul
‡	Cain, Clark L.	St. Paul
‡	Canine, James L.	South St. Paul
‡	Carey, Lewis S.	St. Paul
†‡	Chatterton, Carl C.	St. Paul
‡	Cich, John A.	St. Paul
	Clark, Henry B., Jr.	Minneapolis
‡	Cochrane, Byron B.	St. Paul
	Coddon, Walter D.	St. Paul
‡	Colby, Woodard L.	St. Paul
	Cole, Wallace H.	St. Paul
‡	Coleman, John B.	St. Paul
	Comfort, Thomas H.	St. Paul
‡	Connolly, Coleman J.	St. Paul
	Connolly, Joseph P.	South St. Paul
†	Connor, Charles E.	St. Paul
†‡	Cook, C. Kenneth	St. Paul
‡	Cooper, Charles C.	Moose Lake
†	Countryman, Roger S.	Saratoga, California
‡	Craig, David M.	St. Paul
	Crowley, James H.	St. Paul
‡	Crudo, Vincent D.	St. Paul
	Crum, Arthur Z.	St. Paul
	Crump, James W.	St. Paul
‡	Culligan, John A.	St. Paul
‡	Culver, Lucian G.	St. Paul
‡	Cumming, E. Dale	St. Paul
‡	Davis, Edward V.	St. Paul
	Dawson, James R.	St. Paul
	Decker, Charles H.	St. Paul
†‡	Derauf, Benjamin I.	St. Paul
‡	Derauf, Donald E.	St. Paul
	Derechin, William	St. Paul
‡	Deters, Donald C.	St. Paul
‡	Dinsdale, Howard A.	St. Paul
‡	Drake, Carl B.	St. Paul
	Dunn, Robert C.	St. Paul
‡	Durkin, John L.	St. Paul
	Duvall, Arndt J., III	Minneapolis
‡	Dyrdal, Paul J.	St. Paul
‡	Earl, George A.	St. Paul
‡	Earl, John R.	St. Paul
	Edwards, J. Willard	St. Paul
‡	Edwards, Jesse E.	St. Paul
	Edwards, Lloyd G.	St. Paul
‡	Edwards, Thomas J.	St. Paul
‡	Eelkema, Herman H.	St. Paul
	Eginton, Charles T.	St. Paul
	Eiden, Vera M.	St. Paul
	Emerson, Edward C.	St. Paul
‡	Emmons, Robert W.	St. Paul
‡	Endress, Edward K.	St. Paul
	England, Rodney W.	St. Paul
‡	Enroth, Oscar E.	St. Paul
‡	Erlanson, A. Cornell	St. Paul
‡	Ersfeld, Murray P.	St. Paul
	Falk, Abraham	St. Paul
	Farkas, John V.	St. Paul
‡	Fee, John G.	St. Paul
‡	Felder, Davitt A.	St. Paul
‡	Felion, Arthur J.	St. Paul
‡	Ferguson, John N.	St. Paul
‡	Fesler, Harold H.	St. Paul
‡	Fink, Daniel L.	St. Paul
‡	Fischer, Robert F.	St. Paul
‡	Fisher, Dan W.	St. Paul
‡	Flannery, Hubert F.	St. Paul
	Flom, Reynold P.	St. Paul
‡	Flom, Robert S.	St. Paul
‡	Flynn, Louis L., Jr.	St. Paul
‡	Flynn, Robert A.	St. Paul
*†	Fogarty, Charles W.	St. Paul
†‡	Fogarty, Charles W., Jr.	St. Paul
‡	Fogelberg, Emil J.	St. Paul
†	Foley, Frederic E. B.	St. Paul
	Forsythe, James R.	St. Paul
‡	Fox, LeRoy J.	St. Paul
‡	Freeman, Charles D., Jr.	St. Paul
	Fritz, Wallace L.	St. Paul
‡	Froats, Charles W.	St. Paul
‡	Frye, Charles W.	St. Paul
‡	Fuller, Benjamin F.	St. Paul
	Funke, Joyce L.	St. Paul
‡	Gaertner, Frank M. J., Jr.	St. Paul
‡	Galligan, John J.	St. Paul
	Galway, Charles F.	St. Paul
*†‡	Garbrecht, Arthur W.	St. Paul
‡	Gardner, Walter P.	St. Paul
	Garrow, Douglas M.	St. Paul
	Gaute, Svend T.	St. Paul
‡	Gehlen, Joseph N.	St. Paul
‡	Geist, Robert W.	St. Paul
	Gibbs, Edward C.	St. Paul
	Gilchrist, Milton R.	St. Paul
‡	Gillespie, Delmar R.	St. Paul
‡	Gilsdorf, Donald A.	St. Paul

Continued on Next Page

Ramsey County Medical Society (Continued)

‡	Gleason, Wallace A.	St. Paul
‡	Glenny, William R.	St. Paul
‡	Goldsmith, Joseph W.	St. Paul
*†‡	Goltz, Edward V.	St. Paul
	Goodman, Ernest	St. Paul
‡	Govrik, Kalman	St. Paul
†	Gray, Edward F.	Wauwatosa, Wis.
†	Greenough, William G.	St. Paul
	Gretsch, Gerald A.	St. Paul
	Griffin, Thomas M.	St. Paul
‡	Guenther, Dean E.	West St. Paul
	Guthrie, J. Cameron	St. Paul
‡	Hakanson, Erick Y.	St. Paul
‡	Hall, Barnard	St. Paul
	Hammarsten, James F.	St. Paul
‡	Hammes, Ernest M.	St. Paul
‡	Hammes, Ernest M., Jr.	St. Paul
‡	Hannon, Donald W.	St. Paul
‡	Harmon, Gaius E.	St. Paul
‡	Harris, John E.	Minneapolis
‡	Hartfiel, William F.	St. Paul
	Hartig, Marjorie	St. Paul
†‡	Hauser, Victor P.	St. Paul
‡	Hawkinson, Harlan W.	St. Paul
‡	Hayes, Albert F.	St. Paul
‡	Heck, William W.	St. Paul
†	Hedenstrom, Charles W.	St. Paul
	Hedenstrom, Frank G.	St. Paul
‡	Hedenstrom, Richard H.	St. Paul
	Hedlund, Charles J.	St. Paul
	Heilig, William R.	St. Paul
	Henderson, Terrance P.	White Bear Lake
‡	Hengstler, William H.	St. Paul
‡	Henke, Wilbert J.	St. Paul
‡	Henry, James S.	St. Paul
†	Herman, Samuel M.	Phoenix, Arizona
	Herrick, Donald W.	St. Paul
*	Hertz, Myron J.	St. Paul
‡	Hetzler, John A.	St. Paul
‡	Hilger, Jerome A.	St. Paul
	Hilger, Laurence D.	St. Paul
‡	Hilker, Marcus D.	St. Paul
	Hill, Charlotte W.	St. Paul
	Hiniker, Louis P.	St. Paul
‡	Ho, Shu Kang	St. Paul
‡	Hochfilzer, John J.	St. Paul
	Hodgson, Jane E.	St. Paul
‡	Hohmann, Albert	St. Paul
†	Holcomb, O. William	St. Paul
	Hollinshead, William H.	St. Paul
‡	Holmen, Robert W.	St. Paul
	Holt, John E.	St. Paul
	Hopkins, G. Wendell	Minneapolis
	Horton, Robert R.	Santa Barbara, California
	Houlton, William H.	St. Paul
†	Howard, Merrill A.	St. Paul
‡	Howe, Newell W.	West St. Paul
	Hunter, Murray H.	Farmington
‡	Hunter, Samuel W.	St. Paul
‡	Hurwitz, Milton M.	St. Paul
	Huseby, Thomas L.	St. Paul
‡	Husebye, Kjeld O.	St. Paul
†	Ide, Arthur W.	St. Paul
‡	Jackson, William C.	St. Paul
	James, Ellery M.	St. Paul
‡	James, John W.	St. Paul
‡	Janssen, Martin E.	St. Paul
	Jarvis, Bruce W.	Houston, Texas
	Jarvis, Charles W.	St. Paul
‡	Jastram, Rupert M.	St. Paul
‡	Johanson, Waldemar G.	St. Paul
	Johnson, Carl E.	St. Paul
	Johnson, Carolyn A.	St. Paul
‡	Johnson, Herbert W.	St. Paul
‡	Johnson, Richard J.	St. Paul
‡	Johnson, Thomas E.	St. Paul
	Joseph, Arnold H.	St. Paul
	Kane, Dennis J.	St. Paul
	Kaplan, David H.	Minneapolis
‡	Karon, Everett H.	St. Paul
	Karon, Irvine M.	St. Paul
‡	Kasper, Eugene M.	St. Paul
	Katz, Louis J.	Long Beach, California
‡	Kelly, Albert C.	St. Paul
‡	Kelly, Edward H.	St. Paul
	Kelly, Helen M.	St. Paul
	Kelly, Joseph R.	St. Paul
‡	Kelsey, Chauncey M.	St. Paul
‡	Kenefick, Emmett V.	St. Paul
‡	Kenyon, Thomas J.	St. Paul
†‡	Kesting, Herman	St. Paul
‡	Knutson, Gerhard E.	St. Paul
‡	Knutson, Robert C.	St. Paul
	Kodres, Nina	St. Paul
‡	Kosiak, Michael	St. Paul
	Koza, Donald W.	St. Paul
	Kraatz, Robert W.	St. Paul
	Kramer, James D.	St. Paul
‡	Krezowski, Thomas K.	St. Paul
‡	Kugler, Alex A.	St. Paul
‡	Kuske, Albert W.	St. Paul
‡	Kusske, Bradley W.	St. Paul
‡	Kusske, Douglas R.	St. Paul
†‡	Kvam, Lowell	St. Paul
‡	Lane, Miles I.	White Bear Lake
‡	Lannin, Bernard G.	St. Paul
‡	Lannin, Donald R.	St. Paul
	Lansky, Shirley	St. Paul
‡	Larrabee, Walter F., Jr.	St. Paul
	Larson, Eva Jane Ostergren	St. Paul
‡	Larson, Kenneth R.	St. Paul
‡	Laszewski, Franz von Zelberschwecht	St. Paul
‡	Lawler, Kevin M.	St. Paul
	Lehman, Donald S.	St. Paul
‡	Leick, Richard M.	St. Paul
†	Leitch, Archibald	St. Paul
‡	Leonard, Stanley A.	St. Paul
†	Lepak, John A.	St. Paul
‡	Lerdahl, Kenneth	St. Paul
‡	Lessard, Richard J.	St. Paul
	Leven, N. Logan	St. Paul
‡	Leverenz, Carleton W.	St. Paul
	Levitt, George X.	St. Paul
‡	Lewis, Glenn M., Jr.	St. Paul
	Lewis, Joyce S., Jr.	St. Paul
‡	Lick, Charles L.	St. Paul
‡	Lick, William J., Jr.	St. Paul
‡	Lien, Richard J.	St. Paul
†	Lightbourn, Edgar L.	Hastings
‡	Lilleberg, Norbert J.	St. Paul
‡	Lillie, Andrew R.	St. Paul
‡	Lindell, Robert E.	St. Paul
	Lindquist, Max F.	South St. Paul
	Lindseth, Esten O.	St. Paul
	Lippman, Hyman S.	St. Paul
	Litkewitsch, Helene	St. Paul

Ramsey County Medical Society (Continued)

‡	Loken, Selmer M.	St. Paul
	Lowe, Alexander D.	South St. Paul
*‡	Lowe, Earl R.	South St. Paul
	Lowe, Thomas A.	South St. Paul
‡	Lundholm, Arthur M.	Harris
†	Lunzer, Richard G.	Topeka, Kansas
‡	Lynch, Francis W.	St. Paul
	Lynch, Richard P.	St. Paul
‡	McCain, Donovan L.	St. Paul
	McCarthy, Charles J.	St. Paul
	McClanahan, Thomas S.	White Bear Lake
	McClellan, Robert J.	St. Paul
	McCloud, C. Naumann	St. Paul
	McDaniel, Samuel P.	Lakeville
	McEllistrem, Edward J.	St. Paul
	McEllistrem, Gerald D.	St. Paul
‡	McEwan, Alexander	St. Paul
‡	McGroarty, Brian J.	St. Paul
	McHutchison, Samuel K.	St. Paul
	McKenzie, Eva E.	St. Paul
‡	McNeill, John A.	St. Paul
	MacCornack, Robert L. Jr.	South St. Paul
	Mackoff, Sam M.	Phoenix, Arizona
	Madland, Robert S.	St. Paul
*†‡	Malerich, J. Anthony	South St. Paul
‡	Malerich, J. Anthony, Jr.	West St. Paul
‡	Manlove, Charles H., Jr.	St. Paul
	Marks, Roger W.	St. Paul
‡	Martin, Dwight L.	St. Paul
†‡	Martineau, Joseph L.	St. Paul
‡	Mateo, Guillermo	St. Paul
	Matthews, James H.	Minneapolis
‡	Mazzitello, William F.	St. Paul
‡	Mears, Burtis J.	St. Paul
‡	Medelman, John P.	St. Paul
‡	Melancon, Joseph F.	St. Paul
‡	Menold, William F.	St. Paul
‡	Merrick, Robert L.	St. Paul
‡	Michienzi, Leonard J.	St. Paul
‡	Miller, Albert G.	St. Paul
	Miller, William T.	St. Paul
	Miller, Winston R.	St. Paul
	Miller, Zondal R.	St. Paul
‡	Milnar, Frank J.	St. Paul
	Milroy, Thomas W.	Minneapolis
‡	Mishek, Charles J.	St. Paul
‡	Mitchell, George S.	St. Paul
	Molander, Herbert A.	St. Paul
‡	Monahan, Robert H.	St. Paul
‡	Mooney, Robert D.	St. Paul
†	Moquin, Marie A.	St. Paul
†	Moren, J. Adelaide	White Bear Lake
	Moriarty, M. Berenice	St. Paul
‡	Muchmore, Harold G.	St. Paul
‡	Muller, A. Eugene	North St. Paul
	Mundahl, Harold R.	St. Paul
‡	Murphy, Jack T.	St. Paul
‡	Murray, Roger C.	St. Paul
*‡	Nash, Leo A.	St. Paul
‡	Neher, Frederick J:	St. Paul
	Neibergs, Lydia I.	St. Paul
	Neibergs, Paul	St. Paul
‡	Nelson, Loren E.	St. Paul
*†	Nelson, Louis A.	St. Paul
‡	Nelson, Louis A., Jr.	St. Paul
	Nesvacil, Leon	St. Paul
	Nichols, Thomas O.	St. Paul
‡	Nimlos, Kenneth O.	St. Paul
†	Nimlos, Lenore O.	St. Paul
*‡	Noble, J. Lawrence	St. Paul
‡	Norman, David D.	St. Paul
	Nuebel, Charles J.	Long Beach, California
†	Nye, Katherine A.	St. Paul
	Nye, Lillian L.	St. Paul
‡	O'Brien, John C.	St. Paul
	O'Kane, Thomas W.	St. Paul
‡	O'Malley, Valentine	St. Paul
	O'Neill, Nial C.	St. Paul
†	O'Reilley, Bernard E.	St. Paul
	Ockuly, Orville E.	St. Paul
†	Ogden, Warner	St. Paul
†	Ohage, Justus	St. Paul
‡	Olsen, Ralph L.	St. Paul
	Olson, Barbara F.	South St. Paul
	Olson, Frances P.	Fergus Falls
†	Osekowsky, Henry J.	St. Paul
†‡	Ostergren, Edward W.	St. Paul
‡	Ouellette, Alfred J.	St. Paul
‡	Owens, Frederick M., Jr.	St. Paul
‡	Palm, Neil M.	St. Paul
‡	Paulson, Elmer C.	St. Paul
‡	Paulson, Wallace J.	St. Paul
†	Pearson, Fritz R.	St. Paul
‡	Pearson, Malcolm M.	St. Paul
	Pedersen, Arthur H.	St. Paul
‡	Perry, John F., Jr.	St. Paul
	Peterson, David B.	St. Paul
‡	Peterson, Donald H.	St. Paul
‡	Peterson, Edward A.	St. Paul
‡	Peterson, Harold O.	Minneapolis
	Peterson, Joel L. E.	St. Paul
	Peterson, Roy L.	White Bear Lake
	Pfeiler, Robert C.	St. Paul
	Phillips, Leonard	St. Paul
‡	Plotke, Harry L.	St. Paul
	Polski, Paul G.	South St. Paul
‡	Post, Edmund A.	St. Paul
	Powers, Robert L.	St. Paul
‡	Prentice, Walter B.	St. Paul
‡	Proud, Harry S.	St. Paul
	Quattlebaum, Frank W.	St. Paul
‡	Raaen, Olaf J.	St. Paul
	Rabcevich, Anatole	St. Paul
‡	Ralph, James R.	St. Paul
	Ramlow, Ralph M.	St. Paul
†	Ramsey, Walter R.	St. Paul
	Rasmussen, Ramby C.	St. Paul
‡	Raths, Otto N., Jr.	St. Paul
‡	Ravits, Harold G.	St. Paul
‡	Rea, Charles E.	St. Paul
‡	Redleaf, Paul D.	St. Paul
‡	Reid, James W.	South St. Paul
	Reif, Robert W.	White Bear Lake
	Richards, Albert M.	St. Paul
‡	Richardson, Edward J., Jr.	St. Paul
‡	Rick, Paul F. W.	St. Paul
	Rinkey, Eugene	St. Paul
	Ripple, Rudolph J.	St. Paul
‡	Ritchie, Wallace P.	St. Paul
‡	Ritt, Albert E.	St. Paul
‡	Roach, Charles A.	St. Paul
‡	Roach, Donald E.	St. Paul
	Rolig, David H.	St. Paul
‡	Rollie, Orris O.	St. Paul

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Ramsey County Medical Society (Continued)

‡	Rosenthal, Robert	St. Paul
	Rossing, Robert G.	San Antonio, Texas
‡	Roth, George C.	St. Paul
†‡	Rothschild, Harold J.	St. Paul
‡	Rowe, Clarence J., Jr.	St. Paul
‡	Roy, Philemon C.	St. Paul
†	Ruhberg, George N.	Santa Barbara, California
‡	Rukavina, John G.	St. Paul
‡	Rushay, Arthur J.	White Bear Lake
‡	Rusterholz, Alan P.	St. Paul
†‡	Ryan, John J.	St. Paul
‡	Ryan, Joseph M.	St. Paul
	Sand, Richard E.	St. Paul
‡	Sandkamp, Virgil A.	South St. Paul
*‡	Sarnecki, M. M.	St. Paul
	Scherek, Jerome J.	St. Paul
	Schloff, Ivan	St. Paul
	Schmidt, Herbert W.	St. Paul
	Schmidtke, Reinhardt L.	St. Paul
†	Schoch, Robert B. J.	St. Paul
	Schochet, H. Laurence	St. Paul
†‡	Schons, Edward	Minneapolis
‡	Schroeckenstein, Hugo F.	St. Paul
	Schultz, Donald O.	St. Paul
	Schwyzer, Marquerite	St. Paul
‡	Scott, Eugene E.	St. Paul
	Sekhon, Mohan S.	St. Paul
‡	Sells, Richard J.	St. Paul
‡	Setzer, Hobert J.	St. Paul
	Severson, Donald R.	St. Paul
†	Shannon, William R.	Faribault
‡	Shelander, Marcus I.	St. Paul
†	Shellman, John J.	Pacific Palisades, California
	Shook, Marcus B.	St. Paul
	Short, Marshall H.	St. Paul
	Siegel, Clarence	St. Paul
‡	Simons, Leander T.	St. Paul
	Singer, Benjamin J.	St. Paul
‡	Skinner, Abbott	St. Paul
†	Skinner, Harvey O.	St. Paul
‡	Smiley, Donald P.	St. Paul
‡	Smisek, Elmer A.	St. Paul
	Smith, H. Nippert	St. Paul
‡	Smith, Vernon D. E.	St. Paul
‡	Smith, William T.	St. Paul
†‡	Snyder, George W.	St. Paul
‡	Sohlberg, Olof I.	St. Paul
‡	Sommerdorf, Vernon L.	St. Paul
‡	Sorem, Milton B.	St. Paul
	Soucheray, Philip H.	St. Paul
‡	Souster, Benjamin B.	St. Paul
‡	Sowada, Ernest J.	St. Paul
‡	Sperl, Michael P., Jr.	St. Paul
	Sprafka, Gregory A.	St. Paul
‡	Sprafka, Joseph L.	St. Paul
‡	Spraitz, Anton F, Jr.	St. Paul
	Stein, Robert L.	North St. Paul
‡	Steinberg, Charles L.	St. Paul
‡	Sterner, Donald C.	St. Paul
‡	Sterner, Ernest R.	St. Paul
‡	Sterner, John J.	St. Paul
	Stolpestad, Armer H.	St. Paul
	Straus, Maurice L.	St. Paul
‡	Strem, Edward L.	St. Paul
	Strickland, Martha J. B.	St. Paul
‡	Sturley, Rodney F.	St. Paul
	Sullivan, W. Albert, Jr.	St. Paul
†	Swanson, John A.	St. Paul
‡	Swanson, Lawrence J.	West St. Paul
	Swanson, Ralph H.	West St. Paul
	Swendson, James J.	St. Paul
‡	Swenson, Donald B.	St. Paul
	Tanasichuk, Murray A.	St. Paul
‡	Tani, George	St. Paul
‡	Teisberg, John E.	St. Paul
	Thompson, Floyd A.	St. Paul
	Thompson, Wayne W.	St. Paul
	Thoreson, M. C. Bernice	South St. Paul
‡	Tiffany, Francis B.	St. Paul
‡	Tifft, Cyril R.	St. Paul
‡	Tongen, Lyle A.	St. Paul
‡	Travis, James S.	St. Paul
	Tregilgas, Richard B.	St. Paul
	Tveten, Omar A.	St. Paul
‡	Ubel, Frank A.	St. Paul
	Vail, David J.	St. Paul
	Van Bergen, Frederick H.	Minneapolis
	Varco, Richard L.	St. Paul
‡	Vaughn, C. Gordon	St. Paul
	Veirs, Dean M.	St. Paul
	Veirs, Ruby J. S.	St. Paul
†‡	Venables, Alexander E.	Marysville, Washington
	Venters, Homer D.	St. Paul
‡	Votel, Thomas W.	St. Paul
‡	Waas, Charles W.	St. Paul
‡	Walker, Arthur E.	St. Paul
‡	Wall, James O.	St. Paul
‡	Walsh, Edward F.	St. Paul
‡	Walter, Clarence W.	St. Paul
	Warner, Clyde M.	St. Paul
	Warren, Cecil A.	St. Paul
‡	Watson, P. Theodore	St. Paul
‡	Watson, William H. A.	St. Paul
‡	Watson, William J.	Newport
	Watz, Clarence E.	St. Paul
‡	Webber, Fred L.	St. Paul
‡	Wedes, Deno J.	St. Paul
‡	Weis, Benjamin A.	St. Paul
‡	Weisberg, Maurice	St. Paul
‡	Wenzel, Gilbert P.	St. Paul
	Westermeyer, Joseph J.	St. Paul
‡	Westover, Darrell E.	St. Paul
	Wetteland, Thomas F.	West St. Paul
‡	Wetzel, Earl V.	St. Paul
	Whiting, F. Douglas	St. Paul
†‡	Wier, G. Thomas	St. Paul
‡	Williams, Clayton K.	St. Paul
‡	Williams, George E.	St. Paul
	Williams, Hugh J.	St. Paul
‡	Williams, John A.	St. Paul
	Williams, Richard A.	St. Paul Park
	Wilson, Fred B.	St. Paul
‡	Wilson, J. Allen	St. Paul
‡	Winter, Robert B.	St. Paul
‡	Witthaus, Melvyn E.	St. Paul
	Wolkoff, Hyman J.	St. Paul
	Woodburn, Robert L.	St. Paul
	YaDeau, Richard E.	St. Paul
	Youngren, Everett R.	St. Paul
	Zachman, Leo L.	St. Paul
	Zagaria, James F.	St. Paul
‡	Zarling, Max E.	St. Paul

RANGE MEDICAL SOCIETY

Koochiching, Itasca and the Northern Portion
of St. Louis County
Regular meetings, 6 times a year, 4th Tuesday of the Month
Annual meeting, January
Number of members 107

PRESIDENT	
Will, Charles B.	International Falls
SECRETARY	
Mast, Fredric L.	Chisholm
CORRESPONDING SECRETARY	
Workman, Mrs. Rae	Hibbing

	Addy, Edward R.	Gilbert
‡	Ahola, Kenneth E.	Hibbing
†	Anderson, Richard W.	St. Paul
	Anderson, Russell H.	Virginia
‡	Antonow, Arthur M.	Virginia
	Baich, Velemir M.	Coleraine
	Barnes, Richard E.	Aurora
	Benell, Otto E.	Virginia
†	Binet, Henry E.	Grand Rapids
‡	Birkemeyer, Eugene J.	Ely
‡	Blackmore, Sidney C.	Biwabik
	Bolz, J. Arnold	Grand Rapdis
	Bonner, John L.	Grand Rapids
	Bowen, Robert L.	Hibbing
	Braun, Ohrmundt C.	Grand Rapids
	Brockway, Roger W.	Grand Rapids
†	Cantwell, William F.	International Falls
‡	Chermak, Francis G.	International Falls
‡	Ciriacy, Edward W.	Ely
	Cope, Hershel B.	Virginia
‡	Coy, Douglas J.	Grand Rapids
‡	Crow, George M.	International Falls
	DeMarais, Lloyd C.	Hibbing
	Dobler, Manfred G.	Ely
‡	Eisenman, Walter	Hibbing
†	Engelstad, Wendell P.	Duluth
‡	Erickson, Vernon D.	Grand Rapids
	Evensta, John B.	Grand Rapids
	Ewens, George B.	Virginia
	Ferrell, Clarence R.	Grand Rapids
	Fletcher, Robert H.	Chisholm
‡	Flynn, Bernard F.	Hibbing
‡	French, Bayard T.	Hibbing
	Friedlieb, Oskar P.	Virginia
	Gerend, Thomas J.	Virginia
	Glomstad, Gary B.	Deer River
*†	Goodman, Charles E.	Virginia
†	Graham, Archibald W.	Chisholm
‡	Grahek, Jack P.	Ely
	Grinley, Andrew V.	Grand Rapids
	Haase, Donald D.	Babbitt
‡	Halper, Bernard	Hibbing
	Halverson, Kermit J.	Parkville
‡	Hanover, Ralph D.	International Falls
‡	Hansen, Robert E.	Hibbing
‡	Heiam, William C.	Cook
	Henwood, Wesley C.	Eveleth
	Ireland, Gerald W.	Grand Rapids
	Jacobson, Clarence	Chisholm
	Joffe, Harold H.	Virginia
‡	Johnson, Calvin J.	Grand Rapids
‡	Johnsrud, Luverne W.	Hibbing
	Johnston, H. Wayne	Virginia
	Karges, Laurel E.	Grand Rapids
	Karish, Louis J.	Grand Rapids
	Kelly, Robert T.	Grand Rapids
	Kiesler, Frank, Jr.	Grand Rapids
	Kotchevar, Frank R.	Eveleth
‡	Kruger, Elmer L.	Nashwauk
	Law, Harrison E.	Virginia
	McKenna, John J.	Virginia
‡	McKenna, Maurice J.	Grand Rapids
	McQuoid, David W.	Littlefork
	Malmstrom, John A.	Virginia
	Martinson, Raymond M.	Virginia
‡	Mast, Fredric L.	Chisholm
‡	Miettunen, John B.	Hibbing
	Mock, Charles J.	Virginia
†	Morsman, L. William	Hibbing
‡	Moyer, Richard R.	Hibbing
‡	Muller, John J.	Hibbing
‡	Murray, Robert A.	Hibbing
‡	Neff, Walter S.	Virginia
	Nelimark, Donald R.	Virginia
‡	Nollet, Donald J.	Hibbing
	Owens, Ben P.	Hibbing
‡	Paciotti, Vincent J.	Hibbing
	Parker, Wilbert H.	Chisholm
	Payne, Richard E.	Virginia
	Perpich, Irene Kosiak	Virginia
	Person, Duane F.	Britt
	Peterson, Edward N.	Virginia
	Prlina, Isaac M.	Virginia
†	Rajala, Arnold I.	St. Paul
	Reed, Paul	Virginia
	Richter, David J.	Virginia
	Roth, Albert H.	Deer River
	Rowe, Richard G.	Silver Bay
	Rowles, Everett K.	Coleraine
‡	Salter, Reginald A.	Virginia
‡	Schirber, Martin J.	Grand Rapids
	Schweiger, Theodore R.	Hibbing
	Sher, David A.	Virginia
	Siegel, John S.	Virginia
	Sinamark, Andrew	Hibbing
	Sisler, Clifford E.	Grand Rapids
	Snyker, Omer E.	Ely
	Stolen, Keith H.	Grand Rapids
*†	Strathern, Moses L.	Gilbert
	Summar, M. Thomas	Virginia
‡	Walker, Stuart B.	Aurora
	Walter, Frederick H.	International Falls
	Weir, Matthew J.	Virginia
‡	Werner, Donald L.	Aurora
‡	Wheeler, Gilbert S.	Virginia
‡	Will, Charles B.	International Falls
	Woodruff, Whitney	Virginia
	Wong, Howard H.	Virginia

RED RIVER VALLEY MEDICAL SOCIETY

Kittson, Mahnomen, Marshall, Norman, Pennington, Polk,
Red Lake and Roseau Counties
Regular meetings quarterly
Annual meeting, December
Number of members 62

	PRESIDENT	
	Brown, Glenn W.	Halstad
	SECRETARY	
	Sather, Russell O.	Crookston
	Anderson, Roland G.	Thief River Falls
‡	Anderson, Wallace E.	Clearbrook
	Baab, Robert O.	Crookston
‡	Behr, Orlo K.	Crookston
‡	Berg, Arnold M.	Roseau
†	Bratrud, Edward	Alexandria
	Brink, Adlai A.	Baudette
‡	Brown, Glenn W.	Halstad
	Cameron, John H.	Clovis, New Mexico
‡	Clapp, Hubert D.	Crookston
	Collins, Roger T.	Roseau
	Cotton, Gerald E.	Fosston
‡	Covey, Kenneth W.	Crookston
	Dagg, Earl	Thief River Falls
‡	Dale, Les N.	Hastings
	Davidson, Duane J.	Thief River Falls
‡	Delmore, John L., Jr.	Roseau
†‡	Flancher, Leon H.	Crookston
‡	Foderick, Peter P.	Hallock
‡	Greene, Daniel E.	Warren
‡	Herber, Leo	Thief River Falls
‡	Hirsch, Stanton	Crookston
	Hogan, Henry W., Jr.	Crookston
	Holm, Owen W.	Crookston
‡	Holmstrom, Carle H.	Warren
	Hunt, Vincent R.	Red Lake Falls
	Janecky, Allen G.	Baudette
‡	Jensen, John A.	Crookston
‡	Kinkade, Byron R.	Ada
‡	Klefstad, Lloyd H.	Greenbush
‡	Kostick, William R.	Fertile
	Leonardson, Peter Y.	Red Lake Falls
‡	Loken, Theodore	Ada
†	Lynde, Orrin G.	Los Gatos, California
‡	Martin, George B.	Thief River Falls
	Mercil, Charles B.	Mahnomen
‡	Mercil, William F.	Crookston
†	Nelson, Henry E.	Crookston
‡	Oppegaard, Chester L.	Crookston
	Overland, Arnold J.	Greenbush
‡	Pollman, Stanley E.	Thief River Falls
‡	Pumala, Erven E.	Warren
‡	Scheuneman, Allen F.	Thief River Falls
‡	Roholt, Christian L.	McIntosh
	Rubin, Jacob S.	Crookston
	Sather, Edgar L.	Fosston
‡	Sather, George A.	Fosston
‡	Sather, Richard N.	Fosston
‡	Sather, Russell O.	Crookston
‡	Scheuneman, Allen F.	Thief River Falls
‡	Schnabel, Robert F.	Crookston
‡	Skogerboe, Rudolph B.	Karlstad
‡	Stadem, Clifford J.	Twin Valley
‡	Stewart, Donald E.	Crookston
‡	Thorsgard, Ernest O.	Thief River Falls
	Thysell, Harold R.	Crookston
‡	Uhley, Charles G.	Crookston
‡	Van Rooy, George T.	Thief River Falls
‡	Wendt, H. Paul	Thief River Falls
‡	Wikoff, Howard M.	Crookston

RENVILLE-REDWOOD COUNTY MEDICAL SOCIETY

Renville and Redwood Counties
Regular meetings, third Tuesday of each month
Annual meeting, December
Number of members 16

	PRESIDENT	
	Eilers, William	Redwood Falls
	SECRETARY	
	Hable, Orville	Buffalo Lake
	Alcorn, William J.	.Wabasso
‡	Anderson, Chester A.	Hector
‡	Bingham, George C.	Bird Island
†	Brand, William A.	Redwood Falls
‡	Ceplecha, Stanley F.	Redwood Falls
‡	Cosgriff, James A.	Olivia
	Cosgriff, James A., Jr.	Olivia
‡	Diessner, Ardell W.	Redwood Falls
‡	Fawcett, Arthur M.	Renville
‡	Flinn, James B.	Redwood Falls
*†	Flinn, Thomas E.	Redwood Falls
‡	Furr, Leo O.	Bird Island
	Hable, Orville A.	Buffalo Lake
‡	Johnson, William E.	Morgan
	Lenz, Joseph R.	Morton
‡	Nelson, Glenn E.	Fairfax
‡	Strauchler, John	Belview

RICE COUNTY MEDICAL SOCIETY

Rice County
Regular meetings quarterly
Annual meeting in December
Number of members 30

	PRESIDENT	
	Bauer, Paul G.	Faribault
	SECRETARY	
	Meyer, Richard H.	Faribault
‡	Bauer, Paul G.	Faribault
‡	Beaton, J. Gordon	Northfield
‡	Bruhl, Heinz H.	Faribault
	Buesgens, Ralph H.	Waterville
‡	Engberg, Edward J.	Faribault
	Francis, David W.	Morristown
‡	Good, Roy H.	Northfield
‡	Graham, Asa B.	Faribault
‡	Haas, Jack F.	Northfield
‡	Halvorson, David C.	Northfield
‡	Hanson, J. W.	Northfield
	Kennedy, George L.	Faribault
‡	Kolars, James J.	Faribault
	Lende, Norman	Faribault
	Meyer, Frederick C.	Kenyon
	Meyer, Paul F.	Faribault
	Meyer, Richard H.	Faribault
	Meyer, Robert P.	Faribault
‡	Nuetzman, Arthur W.	Faribault
‡	Orr, Burton A.	Faribault
	Rumpf, Carl W.	Faribault
‡	Rysgaard, George N.	Northfield
‡	Searl, Richard H.	Faribault
‡	Smith, Thorsten	Faribault
‡	Street, Bernard	Northfield
	Studer, Donald J.	Faribault
†	Traeger, Carl A.	Faribault
‡	Watts, George W.	Faribault
‡	Weaver, Paul H.	Faribault
	Zemke, Robert L.	Northfield

ST. LOUIS COUNTY MEDICAL SOCIETY

Carlton, Cook, Lake and Southern portion of
St. Louis County
Regular meetings, second Thursday in each month
except July and August
Annual meeting, second Thursday in January
Number of members 201

	PRESIDENT	
	Walder, Harold J.	Duluth
	SECRETARY	
	Reed, Henry H.	Duluth
	SECRETARY, EXECUTIVE OFFICE	
	Lundgren, Miss Margaret M.	Duluth
‡	Abraham, Arden L.	Duluth
‡	Ahrens, Curtis F.	Duluth
‡	Asta, Joseph J.	Duluth
†	Athens, A. G.	Santa Barbara, California
‡	Atmore, William G.	Duluth
‡	Aufderheide, Arthur C.	Duluth
‡	Backus, Byron C.	Cloquet
‡	Backus, Lloyd B.	Cloquet
‡	Backus, Reno W.	Nopeming
‡	Bagley, Charles M.	Duluth
	Bagley, Elizabeth C.	Duluth
†‡	Bagley, William R.	Duluth
‡	Bakkila, Henry E.	Duluth
‡	Balmer, Albert I.	Duluth
‡	Bardon, Richard	Duluth
‡	Barker, John D.	Duluth
†	Barney, Leon A.	Duluth
‡	Barrett, Earl E.	Duluth
‡	Bartzen, Peter J.	Duluth
‡	Becker, Frederic T.	Duluth
‡	Bell, Harry M.	Duluth
	Bepko, Marie K. (Mrs. Puumala)	Cloquet
	Berdez, George L.	Duluth
‡	Bergan, Robert O.	Duluth
‡	Bianco, Anthony J.	Duluth
‡	Bloom, Joseph	Silver Bay
‡	Boecker, Bernhard	Duluth
	Boman, Paul G.	Duluth
‡	Boyer, Samuel H.	Duluth
‡	Bray, Philip N.	Duluth
‡	Brooker, Warren J.	Duluth
	Brown, Cyrus C.	Duluth
‡	Buckley, Robert P.	Duluth
‡	Butler, John K.	Cloquet
†	Campaigne, Robert J.	Minneapolis
	Chadbourn, Charles R.	Hudson, Wis.
‡	Christensen, Clarence H.	Duluth
†	Chrzan, Donald J.	Colorado Springs, Colorado
	Church, Gerald E.	Two Harbors
	Clark, Elizabeth A. (Mrs. Halbert)	Duluth
‡	Clark, Ivan T.	Duluth
‡	Coll, James J.	Duluth
†	Collins, Arthur N.	Duluth
‡	Conley, Francis W.	Duluth
‡	Coventry, William D.	Duluth
‡	Cowan, George M.	Duluth
‡	Creps, James R.	Duluth
	Davis, William I.	Moose Lake
‡	Deutsch, Robert J.	Duluth
‡	Dickson, Franklin H.	Proctor
‡	Dietrich, Donald E.	Duluth
‡	Dobbs, Richard L.	Duluth
‡	Dwyer, John J.	Duluth
‡	Eckman, Philip F.	Duluth
‡	Eckman, Ralph J.	Duluth
†	Ekblad, John W.	Rock Island, Illinois
‡	Eklund, Carl D.	Duluth
‡	Elias, Frank J.	Duluth
‡	Emanuel, Karl W.	Duluth
	Eppard, Raymond M.	Cloquet

Continued on Next Page

St. Louis County Medical Society (Continued)

	Evison, Emerson O.	Duluth
‡	Fawcett, Keith R.	Duluth
‡	Fellows, Manley F.	Duluth
‡	Feuling, John C.	Duluth
‡	Fifield, Malcolm M.	Duluth
‡	Fischer, Mario M.	Duluth
‡	Fisketti, Henry	Duluth
‡	Fuller, Josiah	Duluth
‡	Gillespie, Malcolm G.	Duluth
†	Gobel, Fredarick L.	Minneapolis
‡	Goldish, Daniel R.	Duluth
‡	Goldish, Robert J.	Duluth
‡	Goldschmidt, Volker	Duluth
‡	Goodnow, William H.	Duluth
‡	Gowan, Lawrence R.	Duluth
‡	Grohs, William H.	Duluth
‡	Gronquist, Y. K. J.	Cloquet
‡	Haavik, John E.	Duluth
	Halbert, John J.	Duluth
‡	Halliday, Phillip V.	Duluth
	Hanson, Ernest O.	Cloquet
‡	Harrington, Vernon A.	Duluth
*†‡	Hatch, Walter E.	Duluth
†‡	Helwig, Karl L.	Duluth
‡	Hilding, Anderson C.	Duluth
†	Hill, Frederick E.	Riverside, California
†	Hirschboeck, Frank J.	Duluth
‡	Hoeg, Dwight C.	Duluth
‡	Hoff, Herbert O.	Duluth
‡	Houkom, S. Sverre	Duluth
	Hutchinson, Henry	Moose Lake
	Jacklin, Alexander J.	Duluth
‡	Jacobson, Ferdinand C.	Duluth
†	Jensen, Thorvold J.	Duluth
‡	Jeronimus, Henry J.	Duluth
	Jessico, Charles M.	Duluth
‡	Johnson, Franklin L.	Duluth
‡	Johnson, Karl E.	Duluth
	Johnson, Theodore L.	Duluth
†	Jorgenson, Edward O.	Rochester
‡	Juntunen, Roy R.	Duluth
†‡	Klein, Harry	Duluth
‡	Klein, William A.	Duluth
‡	Knoedler, John P.	Duluth
	Kohlbry, Carl O.	Duluth
	Kosiak, William	Two Harbors
‡	Krueger, Victor R.	Nopeming
‡	L'Abbe, A. J. Philip	Duluth
	L'Esperance, Bernard F.	Two Harbors
	LaBree, Robert H.	Duluth
*†‡	Laird, Arthur T.	Duluth
‡	Langseth, Rodney N.	Duluth
‡	Larson, Donald M.	Duluth
	Larson, Keith D.	Moose Lake
‡	Latterell, Kenneth E.	Duluth
‡	Leek, Joseph H.	Duluth
†	Lepak, Francis J.	Duluth
	Leppink, Harold B.	Two Harbors
	Leppo, N. Erkki A.	Duluth
	Linke, Charles A.	Duluth
	Linke, Clara L.	Duluth
‡	Litman, Samuel N.	Duluth
†‡	McNutt, John R.	Duluth
	MacDonald, Roger A.	Grand Marais
‡	MacRae, Gordon C.	Duluth
†‡	Magney, Fredolph H.	Duluth
	Martin, Webster C.	Duluth
‡	Martin, William B.	Dayton, Ohio
‡	Maryland, Daniel L.	Duluth
†	Mayne, Roy M.	St. Paul
‡	Merrick, William G.	Duluth
‡	Meyer, Howard J.	Duluth
	Moe, Thomas	Moose Lake
	Monge', James J.	Duluth
‡	Monserud, Nels O.	Cloquet
‡	Moyer, John B.	Duluth
‡	Munger, James E.	Duluth
	Munson, Martin S.	Moose Lake
‡	Nisius, George F.	Duluth
‡	Nisswandt, Albert L.	Duluth
†‡	Norberg, Carl E.	Cloquet
*‡	Nutting, Roland E.	Duluth
‡	O'Neill, John C.	Duluth
*‡	Olson, Albert E.	Duluth
‡	Olson, Archie O.	Duluth
‡	Parson, E. Irvine	Duluth
‡	Pasek, Antone W.	Cloquet
‡	Patch, Orien B.	Duluth
‡	Pedersen, Roy C.	Duluth
‡	Petersen, John H.	Duluth
‡	Pollard, William S.	Duluth
*†	Power, John E.	Duluth
‡	Power, John E., Jr.	Duluth
	Puumala, Barbara M.	Cloquet
	Puumala, Reino H.	Cloquet
	Puumala, Ricard R.	Cloquet
‡	Reardon, Andrew E.	Duluth
‡	Reed, Henry H.	Duluth
	Rondeau, Eugene T.	Two Harbors
‡	Rudie, Peter S.	Duluth
‡	Rudie, William D.	Duluth
‡	Runquist, John M.	Duluth
‡	Ruth, Bradley R.	Duluth
	Ryan, Edward A.	Duluth
	Sach-Rowitz, Alvan	Moose Lake
	Saloum, Lucille M.	Duluth
	Sanford, John B.	Duluth
†	Sarff, Oliver E.	Duluth
	Sax, Milton H.	Duluth
	Sax, Simon G.	Duluth
‡	Schmid, John F.	Duluth
‡	Schneider, Lawrence E.	Duluth
*†	Schroder, Charles H.	Pottstown, Pennsylvania
‡	Shirley, Raymond M.	Duluth
	Slack, William J.	Duluth
‡	Smith, Cyril M.	Duluth
	Smith, Wallace R.	Grand Marais
‡	Spang, Anthony J.	Duluth
‡	Spang, James S.	Duluth
‡	Spang, W. M.	Duluth
‡	Stein, William A.	Duluth
‡	Storsteen, Kenneth A.	Duluth
‡	Streitz, John M.	Duluth
‡	Strewler, Gordon J.	Duluth
‡	Swedberg, William A.	Duluth
	Swensen, Don P.	Duluth
‡	Swenson, Arnold O.	Duluth
‡	Teich, Kenneth W.	Duluth
‡	Terrell, Bernard J.	Nopeming
‡	Tetlie, James P.	Duluth
‡	Thomas, John V.	Duluth
‡	Thurn, Roy J.	Duluth
‡	Tosseland, Noel E.	Duluth
†	Trautmann, James C.	Rochester
‡	Tuura, James L.	Edmonds, Washington
	Van Druten, William A.	Duluth

St. Louis County Medical Society (Continued)

†	Van Puffelen, Paul S.	Rochester
	Van Ryzin, Donald J.	Duluth
‡	Walder, Harold J.	Duluth
‡	Wall, Jack E.	Duluth
‡	Wallace, Martin O.	Duluth
‡	Wells, Arthur H.	Duluth
‡	Williams, Bruce F. P.	Duluth
†	Winter, John A.	Duluth
‡	Wolfe, John W.	Duluth
‡	Young, Hadley R.	Duluth
‡	Young, Thomas O.	Duluth
‡	Zemmers, Robert	Duluth

SCOTT-CARVER COUNTY MEDICAL SOCIETY

Scott and Carver Counties
Regular meetings, 1st Tuesday of each month
Annual meeting in December
Number of members 42

PRESIDENT
Lehrer, Alfred J., Jr. .... Montgomery
SECRETARY
Nelson, Gerald E. .... Chaska

‡	Adams, Patrick J.	Shakopee
‡	Bean, Charles N.	Waconia
‡	Bratholdt, James W.	Watertown
†	Buck, Frederick H.	Shakopee
‡	Cervenka, Charles F.	New Prague
‡	Clarke, John W.	Waconia
†‡	Daly, Alfred E.	Montgomery
‡	Doherty, Elmer M.	New Prague
	Erickson, Robert L.	Rosemount
‡	Field, Anthony H.	Savage
‡	Hallgren, Roger B.	Belle Plaine
†‡	Hebeinsen, Milton B.	Chaska
	Heinz, Ivy	Shakopee
‡	Heinzerling, Carl R.	Chaska
†‡	Juergens, Herman M.	Belle Plaine
	Kleinsasser, Warren L.	Farmington
	Kucera, Stanley T.	Northfield
‡	Kuz, Eugene	Savage
‡	Larson, Leighton W.	Waconia
‡	Lehrer, Alfred J., Jr.	Montgomery
‡	Lukk, Olaf	Prior Lake
‡	Moller, Jurgen	Farmington
‡	Nelson, Gerald E.	Chaska
†	Novak, Edward E.	New Prague
‡	Olson, Richard E.	Chaska
‡	Pearson, Bror F.	Shakopee
‡	Philp, David R.	Watertown
‡	Pistulka, R. D.	Chaska
‡	Ponterio, James E.	Shakopee
‡	Prespare, Charles	Waconia
	Rieschl, Elizabeth K.	Jordan
‡	Rynda, Edwin R.	New Prague
‡	Schimelpfenig, George T.	Chaska
‡	Schwartz, Robert K.	Chaska
‡	Spagnolo, Anthony A.	Shakopee
	Splettstoesser, Robert W.	Belle Plaine
	Stahler, Paul A.	Jordan
‡	Tuma, Ben	Waconia
‡	Wempner, Jon D.	Waconia
†‡	Westerman, Alvin S.	Montgomery
†‡	Westerman, Fred C.	Montgomery
‡	Whitesell, Lloyd A., Jr.	Shakopee

SOUTHWESTERN MINNESOTA MEDICAL SOCIETY

Cottonwood, Jackson, Murray, Nobles, Pipestone
and Rock Counties
Regular meetings 1st Monday of each month except
July and August
Annual meeting, November
Number of members 60

PRESIDENT
Buresh, Kenneth .... Westbrook
SECRETARY
Heiberg, O. M. .... Worthington

‡	Amick, Arthur E.	Worthington
‡	Bader, J. L.	Slayton
	Basinger, Harold P.	Windom
	Basinger, Homer P.	Windom
‡	Beckering, Gerrit	Edgerton
‡	Beckering, Roland G.	Edgerton
‡	Benjamin, Walter G.	Pipestone
‡	Bofenkamp, Ferdinand W.	Luverne
‡	Boone, Ervin S.	Luverne
	Boyd, Frank E.	Pipestone
	Buresh, Kenneth L.	Westbrook
‡	Carlson, John V.	Westbrook
‡	Carlson, Lloyd E.	Worthington
‡	Christiansen, Harold A.	Jackson
‡	Dawson, Lorin D.	Worthington
‡	Desai, B. J.	Worthington
	Dokken, James H.	Windom
‡	Doman, Victor W.	Lakefield
	Fitch, Charles G.	Worthington
†‡	Halloran, Walter H.	Jackson
‡	Halpern, David J.	Brewster
‡	Harrison, Percy W.	Worthington
	Hegstad, Thomas C.	Windom
‡	Heiberg, Olaf M.	Worthington
	Hoyer, Ludolf J.	Windom
†	Jaeger, Dwight E.	Minneapolis
	Johnson, Alan R.	Windom
‡	Keyes, Robert W.	Pipestone

Continued on Next Page

Southwestern Minnesota Medical Society (Continued)

‡	Kilbride, Edwin A.	Worthington
†	Koos, Gerald W.	Minneapolis
‡	Kotval, Russell J.	Pipestone
‡	Laikola, Leslie A.	Adrian
‡	Larsen, Russell H.	Lakefield
‡	Lohmann, John G.	Pipestone
‡	Maitland, Edwin T.	Jackson
	Martin, Albert	Luverne
	McNear, George R., Jr.	Heron Lake
‡	Minge, Raymond K.	Worthington
‡	Nealy, Donald E.	Adrian
‡	Nywall, Dean D.	Slayton
‡	Odland, Donald M.	Luverne
‡	Patterson, Hugh D.	Slayton
‡	Pierce, Robert B.	Mountain Lake
‡	Pierson, Roy F.	Slayton
†‡	Piper, William A.	Mountain Lake
‡	Plucker, Milton W.	Worthington
	Rud, Paul D.	Luverne
	Ryding, Vincent	Ames, Iowa
‡	Schade, Frederick L.	Worthington
‡	Seisler, Edward P.	Worthington
†‡	Sherman, Charles L.	Luverne
‡	Stam, John	Worthington
	Strand, Jack W.	Jasper
	Stratte, Harold C.	Windom
†	Sundberg, A. Bruce	Minneapolis
‡	Vandersluis, Charles W.	Minneota
†‡	Vix, Vernon A.	Minneapolis
‡	Wells, Walter B.	Jackson
	Wiens, Alvin L.	Mountain Lake
†	Williams, Charles A.	Seattle, Washington

STEARNS-BENTON COUNTY MEDICAL SOCIETY

Stearns and Benton Counties
Regular meetings third Thursday of the month
Annual meeting December
Number of members 83

PRESIDENT

Petersen, Robert T. .... St. Cloud

SECRETARY

Sommers, Stephen D. .... St. Cloud

‡	Alden, Charles W.	Kimball
	Aulick, Ernest J.	Paynesville
‡	Autrey, William A.	St. Cloud
	Ballantine, Jerome J.	St. Cloud
	Barnett, Arthur J.	Foley
‡	Baumgartner, Florian H.	Albany
‡	Berger, Phil R.	St. Cloud
‡	Beuning, John B.	St. Cloud
‡	Bozanich, Milosh S.	St. Cloud
‡	Brigham, Charles F., Jr.	St. Cloud
‡	Broker, Henry M.	St. Cloud
	Brown, Frank T.	St. Cloud
†	Buscher, Julius C.	St. Cloud
	Carter, Donald C.	St. Cloud
‡	Cesnik, Robert J.	Sauk Rapids
†	Clark, Harry B.	St. Cloud
	Cleaves, William D.	Sauk Centre
	Cumming, Robert	St. Cloud
	Dehnel, Luther L.	St. Cloud
‡	Donaldson, Charles S.	St. Cloud
	DuBois, Julian F.	Sauk Centre
‡	Evans, Leslie M.	Sauk Rapids
‡	Gaida, Joseph B.	St. Cloud
	Gersterkorn, George B.	Milaca
	Goehrs, Gilman H.	St. Cloud
*†	Haberman, Emil	Osakis
	Halenbeck, Philip L.	St. Cloud
	Harbaugh, John T.	St. Cloud
	Hedenstrom, Paul H.	St. Cloud
†	Henry, Clarence J.	Onamia
	Henry, Joseph E.	Milaca
	Higdon, Donald A.	St. Cloud
	Hughes, Bernard J.	St. Cloud
†‡	Jones, Richard N.	St. Cloud
	Keith, Paul J.	Milaca
‡	Kelly, James H.	St. Cloud
‡	Kelly, John F.	Cold Spring
*‡	Kline, Richard F.	St. Cloud
	Koenig, Robert P.	St. Cloud
	Kuhlmann, Lawrence B.	Melrose
	Kvistberg, Gerald K.	St. Cloud
‡	LaFond, Edward M.	St. Cloud
‡	Lenarz, Albert J.	St. Cloud
	Lindeman, Raymond J.	Paynesville
‡	Lindley, Stanley B.	St. Cloud
	Loeb, George	St. Cloud
‡	Loes, Louis A.	St. Cloud
†‡	McDowell, John P.	St. Cloud
	McGovern, William A.	St. Cloud
	McNamara, John P.	Rice
	May, Robert B.	St. Cloud
‡	Milhaupt, Emmett N.	St. Cloud
	Mueller, Rudolph B.	Richmond
‡	Murn, Thomas G.	St. Cloud
	Murray, Robert	St. Cloud
‡	Musachio, Nicholas F.	St. Paul
	Myre, Clifford R.	Paynesville
	Neils, Vernon E.	St. Cloud
	Nietfield, Aloys B.	Sauk Centre
	O'Keefe, James P.	St. Cloud
‡	Olinger, John N.	St. Cloud
‡	Petersen, Robert T.	St. Cloud
‡	Phares, Otto C.	St. Cloud
‡	Raetz, Sylvester J.	Maple Lake
‡	Reif, Henry J.	St. Cloud
	Rice, William H.	St. Cloud
‡	Richards, William B.	St. Cloud
	Rozycki, Anthony T.	St. Cloud
	Salk, Richard J.	Albany
	Savelkoul, Gene R.	Belgrade
‡	Schmitz, Everett J.	St. Cloud
	Smith, J. Weston	St. Cloud
‡	Sisk, Harvey E.	St. Cloud
	Sommers, Stephen D.	St. Cloud
‡	Stiles, Clifford D.	Foley
	Thienes, R. Lawrence	St. Cloud
	Thuringer, Carl B.	St. Cloud
	Undem, Dale	St. Cloud
‡	Vanderpool, Thomas E.	Paynesville
	Veranth, Leonard A.	St. Cloud
‡	Wenner, Waldemar T.	St. Cloud
‡	Wittrock, Louis H.	Watkins
	Zachman, Albert H.	Melrose
	Zachman, John F.	Melrose
	Zeleny, Joseph W.	St. Cloud

STEELE COUNTY MEDICAL SOCIETY

Steele County
Regular meetings, Third Tuesday of every other month
Annual meeting, January
Number of members 23

	PRESIDENT	
	Halvorsen, Daniel K.	Owatonna
	SECRETARY	
	Henry, John C.	Owatonna
‡	Anderson, Franklin C.	Owatonna
	Arnesen, John F.	Owatonna
‡	Bush, Roger A.	Owatonna
‡	deWerd, Robert W.	Owatonna
	Dewey, Donald H.	Owatonna
‡	Fischer, John R.	Blooming Prairie
‡	Floersch, Adrian J.	Owatonna
‡	Halvorsen, Daniel K.	Owatonna
	Hartung, Elmer H.	Claremont
‡	Henry, John C.	Owatonna
‡	Henry, Kenneth G.	Owatonna
‡	Hilker, Robert T.	Owatonna
	Honath, Donald H.	Owatonna
	Kulstad, Oscar S.	Dodge Center
	Lundquist, Curt W.	Owatonna
‡	McEnaney, James E.	Owatonna
†	McIntyre, John A.	Owatonna
†	Morehead, Dewey E.	Bodega Bay, California
‡	Olson, Albert J.	Owatonna
	Roberts, Oliver W.	Owatonna
	Schaefer, Joseph F.	Owatonna
	Stransky, Theodore W.	Owatonna
†	Wilkowske, Rudolph J.	Owatonna

UPPER MISSISSIPPI MEDICAL SOCIETY

Aitkin, Beltrami, Cass, Clearwater, Crow Wing, Hubbard,
Lake of the Woods, Morrison, Todd and Wadena Counties
Regular meetings three times yearly
Annual meeting January
Number of members 99

	PRESIDENT	
	Pedersen, Robert L.	Brainerd
	SECRETARY	
	Anderson, Arden O.	Brainerd
‡	Adkins, James T.	Bertha
‡	Aga, John H.	Brainerd
‡	Anderson, Arden O.	Brainerd
	Anderson, Werner W.	Brainerd
†‡	Badeaux, George I.	Brainerd
	Belcher, Royden A.	Little Falls
‡	Bender, James H.	Brainerd
‡	Benson, Alfred H.	Little Falls
‡	Bissinger, Lester L.	Brainerd
†‡	Bolstad, Owen C.	Fort Snelling
‡	Borgerson, Arthur H.	Long Prairie
‡	Brown, Russell T.	Browerville
	Burman, Richard E.	Aitkin
‡	Cardle, George E.	Brainerd
	Closuit, Frederick C.	Aitkin
‡	Coombs, Carl H.	Cass Lake
†	Craig, C. C.	International Falls
‡	Crow, Earl R.	Minnetonka
	Davis, Lloyd T.	Wadena
	Davis, Luther F.	Wadena
	Deweese, Wilford J.	Bemidji
†	Dillenburg, C. J.	Grand Forks, N. D.
‡	Dodson, Albertus F.	Brainerd
†‡	Duthoy, E. J.	Bloomington
‡	Erickson, Alvin O.	Long Prairie
‡	Fitzsimons, William E.	Brainerd
	Fortier, George M. A.	Little Falls
	Franklin, Gordon W.	Northome
‡	Gamm, Edgar R.	Park Rapids
†	Ghostley, Mary C.	Minneapolis
	Gregoire, Earl	Bemidji
	Griffin, John W.	Bemidji
	Grimes, Paul T.	Park Rapids
	Groschupf, Richard P.	Bemidji
†	Groschupf, Theophilus P.	Bemidji
‡	Grose, Frederick N.	Clarissa
	Hall, George M.	Bemidji
	Halme, William B.	Wadena
	Hansen, Milo L.	Little Falls
	Hartjen, Jason K.	Bemidji
	Haugen, Norman R.	Park Rapids
†	Healy, Raymond T.	Pierz
‡	Heid, James K.	Little Falls
	Hendricks, Esten J.	Verndale
	Henry, Richard T.	Crosby
	Hildebrand, John E.	Bemidji
	Hoganson, Donald E.	Bemidji
‡	Johnson, Douglas L.	Little Falls
†	Johnson, Einer W.	Bemidji
‡	Kanne, Earl R.	Brainerd
‡	Kelley, Roger E.	Crosby
	Knipp, William J.	Brainerd
	Knoll, W. V.	Brainerd
	Larson, Leroy J.	Bagley
‡	Lee, Hubert W.	Brainerd
†	Lofstrom, Dennis E.	St. Paul
	Longfellow, Helen W.	Brainerd
	Lund, Werner J.	Staples
	Lundsten, Leslie C.	Bemidji
‡	McLane, William O.	Brainerd
‡	Marshall, Clark N.	Crosby
‡	Marvin, Joseph E.	Brainerd
‡	Meller, Maurice	Brainerd
	Mortenson, Howard O.	Menahga
‡	Mosby, Maurice E.	Long Prairie
‡	Mulligan, Arthur M.	Brainerd
	Murtaugh, Robert J.	Wadena
	Ness, Duane E.	Wadena
‡	Nixon, James B.	Crosby
	Nordlund, Mildred E.	McClellan A.F.B. Calif.
‡	O'Leary, John B.	Brainerd
	Olson, Lillian A.	Bemidji
	Palmer, Harry A.	Blackduck
	Parker, Charles W.	Wadena

Continued on Next Page

Upper Mississippi Medical Society (Continued)

Parker, Philip J.	Staples
Parker, Warren E.	Sebeka
‡ Pedersen, Robert L.	Brainerd
‡ Pelzl, Charles R.	Pine River
Petraborg, Harvey T.	Aitkin
Pettersen, George R.	Aitkin
‡ Poppie, Robert W.	Brainerd
‡ Reichelderfer, Charles F.	Staples
‡ Reichelt, Leland G.	Wadena
‡ Ringle, Otto F.	Walker
Roholt, Hartvig B.	Bemidji
† Schulberg, Verne A.	Minneapolis
Seifert, Donald R.	Little Falls
Spieler, F. B.	Pequot Lakes
‡ Stein, Raymond J.	Pierz
‡ Stoy, Robert A.	Little Falls
† Thompson, James R.	Rochester
‡ Troyer, Richard C.	Brainerd
† Ulrich, Emery E.	Oklahoma City, Oklahoma
*†‡Watson, Alexander M.	Royalton
‡ Watson, Sidney W.	Royalton
‡ Westley, Kent F.	Little Falls
Whittemore, Dexter D.	Bemidji
† Will, William W.	Bertha
Williams, Mervyn M.	Ah-Gwah-Ching
Witter, Robert L.	Wadena

WABASHA COUNTY MEDICAL SOCIETY

Wabasha County
Regular meetings, special call
Annual meeting first Thursday after first Monday in October
Number of members 14

PRESIDENT	
Bayley, E. Covell	Lake City
SECRETARY	
Gjerde, William P.	Lake City
‡ Bayley, E. Covell	Lake City
‡ Bouquet, Bertram J.	Wabasha
‡ Bowers, Robert N.	Lake City
‡ Ekstrand, LeRoy M.	Wabasha
‡ Ellis, Earl W.	Elgin
‡ Flatt, John R.	Wabasha
‡ Gjerde, William P.	Lake City
†‡ Habein, Harold C.	Wabasha
‡ Mahle, Donald G.	Plainview
Martin, David	Wabasha
Martin, Doreen A.	Pepin, Wisconsin
Ochsner, Clarence G.	St. Paul
† Replogle, William H.	Los Angeles, California
‡ Sontag, David W.	Lake City

WASECA COUNTY MEDICAL SOCIETY

Waseca County
Annual meeting, January
Number of members 9

PRESIDENT	
Hottinger, Raymond C.	Janesville
SECRETARY	
Campbell, Wayne L.	Waseca
‡ Campbell, Wayne L.	Waseca
‡ Davis, Raymond D.	Naples, Florida
‡ Hottinger, Raymond C.	Janesville
‡ Normann, Stephen T., Jr.	Waseca
‡ Oeljen, Siegfried C. G.	Waseca
‡ Olds, George H.	New Richland
‡ Rohrer, Thomas P.	Waseca
‡ Stover, Laddie E.	Waseca
‡ Swenson, Orvie J.	Waseca

WASHINGTON COUNTY MEDICAL SOCIETY

Washington and Dakota Counties
Regular meetings, second Tuesday in each month
Annual meeting, December
Number of members 28

PRESIDENT	
McCarten, Francis M.	Stillwater
SECRETARY	
Bealka, Neal M.	Stillwater
‡ Bealka, Neil	Stillwater
Brabec, Paul F.	Hastings
‡ Carlson, Russel E.	Stillwater
† Cottor, Robert E.	St. Paul
Fasbender, Herman T.	Hastings
† Holcomb, Joel T.	Marine-on-St. Croix
‡ Jenson, James E.	Stillwater
‡ Johnson, Emil	Stillwater
‡ Johnson, O. Guy	Bayport
Johnson, Robert H.	Bayport
‡ Juergens, Manley F.	Stillwater
Just, Herman J.	Hastings
‡ Kiolbasa, Edward B.	Stillwater
Kulzer, Norbert J.	Hastings
‡ McCarten, Francis M.	Stillwater
Midboe, Gilbert T.	Forest Lake
‡ Murphy, Thomas R.	Stillwater
Peikert, Carl F.	Forest Lake
Peterson, John O.	Hastings
Petroske, James L.	Hastings
† Poirier, Joseph A.	Forest Lake
‡ Ruggles, George M.	Forest Lake
‡ Sherman, Carnot H.	Bayport
‡ Stratte, Jon R.	Stillwater
†‡ Stuhr, John W.	Stillwater
† Torghele, John R.	Hastings, Nebraska
Van Meier, Henry	Stillwater
Weiss, Carl A.	Hastings

WEST CENTRAL MINNESOTA MEDICAL SOCIETY

Big Stone, Pope, Stevens and Traverse Counties
Regular meetings, second Tuesday in March, May, September and November
Annual meeting, November
Number of members 28

PRESIDENT
Watson, Robert M. .... Morris
SECRETARY
Rossberg, Raymond A. .... Morris
‡ Arneson, Arthur I. .... Morris
†‡ Behmler, Frederick W. .... Morris
† Bergan, Otto .... Clinton
‡ Brace, Ray I. .... Clinton
‡ Bucher, Foster D. .... Starbuck
‡ Christenson, Carl E. .... Clinton
*†‡Eberlin, Edward A. .... Glenwood
‡ Eide, O. A. .... Hancock
‡ Hedemark, Homer H. .... Ortonville
Hedemark, Truman A. .... Ortonville
‡ Karn, Jacob F. .... Ortonville
Knip, Robert J. .... Ortonville
Kolp, Berton A. .... Glenwood
‡ Kooda, Jennings C. .... Morris
‡ Kozel, William J. .... Morris
‡ Lee, Gordon E. .... Glenwood
†‡ Letson, Robert D. .... Minneapolis
‡ Lindberg, Alfred L. .... Wheaton
‡ Magnuson, Allen E. .... Wheaton
‡ Merrill, Robert W. .... Morris
‡ Oliver, Irwin L. .... Graceville
‡ Popoff, Russel G. .... Graceville
‡ Rossberg, Raymond A. .... Morris
Schuft, James R. .... Morris
‡ Swedenburg, Paul A. .... Glenwood
‡ Vangerud, Paul T. .... Wheaton
‡ Watson, Robert M. .... Morris
‡ Winge, Herbert C. .... Wheaton
‡ Zempel, Alan R. .... Starbuck

WINONA COUNTY MEDICAL SOCIETY

Winona County
Regular meetings, second Monday in January, April, July and October
Annual meeting, January
Number of members 33

PRESIDENT
Fenske, Arnold .... Winona
SECRETARY
Heise, Herbert vR. .... Winona
‡ Boardman, Dalmon V. .... Winona
‡ Christensen, Eli E. .... Winona
‡ Degallier, Daniel .... Winona
‡ Fenske, Arnold .... Winona
‡ Finkelnburg, William .... Winona
‡ Garber, George L. .... Winona
‡ Haesly, Warren W. .... Winona
‡ Hartwich, Roger F. .... Winona
‡ Hawk, Dale J. .... St. Charles
‡ Heise, Carl vR. .... Winona
‡ Heise, Herbert vR. .... Winona
‡ Heise, Paul vR. .... Winona
Heise, Philip vR. .... Winona
‡ Heise, William vR. .... Winona
‡ Hughes, Sidney O. .... Winona
‡ Johnson, Curtis M. .... Winona
‡ Johnston, Leonard .... Winona
†‡ Keyes, John D. .... Winona
‡ Loomis, George L. .... Winona
†‡ McLaughlin, Edmund M. .... Winona
‡ Mattison, Percy A. .... Winona
‡ Meinert, Albert E. .... Winona
‡ Peterson, John R. .... Rushford
‡ Roemer, Henry J. .... Winona
‡ Rogers, Charles W. .... Winona
†‡ Schmidt, Hilmar R. .... Rushford
‡ Testor, James V. .... Winona
‡ Tweedy, John A. .... Winona
‡ Tweedy, Robert B. .... Winona
‡ Vollmer, Frederick J. .... Winona
‡ Wilson, L. J. .... Rushford
‡ Wilson, R. H. .... LaMoille
‡ Younger, Lewis I. .... Winona

WRIGHT COUNTY MEDICAL SOCIETY

Wright County
Regular meetings, 1st Tuesday of every month
Annual meeting in November
Number of members 14

PRESIDENT
Sandeen, R. M. .... Buffalo
SECRETARY
Maus, Donald .... Monticello
‡ Anderson, Waldo P. .... Buffalo
‡ Bendix, Lester H. .... Annandale
† Catlin, John J. .... Macomb, Illinois
‡ Catlin, Theodore J. .... Buffalo
†‡ Ellison, Frank E. .... Monticello
‡ Greenfield, William T. .... Cokato
‡ Guilfoile, Pierre J. .... Delano
‡ Hart, William E. .... Monticello
‡ Maus, Donald J. .... Monticello
‡ Purves, G. Harland .... Buffalo
‡ Sandeen, Robert M. .... Buffalo
Shin, Rok .... Howard Lake
‡ Smorstok, Matthew B. .... Monticello
‡ Thielen, Robert D. .... St. Michael

ZUMBRO VALLEY MEDICAL SOCIETY

Olmsted, Houston, Fillmore and Dodge Counties
Regular meetings, 1st Wednesday of every odd-numbered month
Annual meeting, November
Number of members 798

	PRESIDENT	
	Diessner, G. Roy	Rochester
	SECRETARY	
	Campbell, Malcolm	Rochester
	EXECUTIVE SECRETARY	
	Fricke, Robert E.	Rochester
‡	Aaro, Leonard A.	Rochester
	Adler, Franz A.	Rochester
‡	Adson, Martin A.	Rochester
‡	Affeldt, Daniel E.	Kasson
†‡	Ahlfs, Jacob J.	Minnetonka
†	Ahmann, David L.	Rochester
†	Aldrete, Joaquin S.	Rochester
#	Allen, Charles V.	Modesto, Calif.
†	Allocco, Dominic J.	Rochester
†	Amberg, Samuel	Rochester
‡	Andersen, Howard A.	Rochester
†	Andersen, Robert L.	Rochester
†	Anderson, Dale L.	Rochester
†‡	Anderson, Mark J.	Rochester
‡	Anderson, Markham J., Jr.	Rochester
‡	Anderson, Milton W.	Rochester
†	Andreini, Paul H.	Rochester
†	Angros, Richard H.	Rochester
†	Anquist, Kenneth A.	Rochester
†	Anzalotta-Hernandez, Jose	Rochester
	Appleman, Robert M.	Rochester
	Archambeau, Paul L.	Sebastopol, Calif.
†	Arnold, Gordon B.	Rochester
†	Atwood, Roger M.	Rochester
†	Auger, Armand J.	Rochester
‡	Baars, Conrad W.	Rochester
†	Babb, Richard R.	Rochester
‡	Baggenstoss, Archie H.	Rochester
‡	Bair, Hugo L.	Rochester
	Baird, Raymond L.	Harmony
†	Baitz, Thomas	Rochester
¶	Bajec, Dusan	Poljane, Yugoslavia
‡	Baker, George S.	Rochester
†	Baker, Harry R.	Hayfield
‡	Baker, Hillier L., Jr.	Rochester
†	Baker, James A.	Rochester
	Balfour, William M.	Lawrence, Kansas
†	Banaszak, Edward F.	Rochester
#	Banitt, Louis W.	A.P.O., New York
‡	Banner, Edward A.	Rochester
†	Bard, James W.	Rochester
†‡	Barker, Nelson W.	Rochester
†	Barnes, Arlie R.	Rochester
‡	Barry, Maurice J., Jr.	Rochester
‡	Bartholomew, Lloyd G.	Rochester
‡	Bastron, James A.	Rochester
‡	Bayrd, Edwin D.	Rochester
	Beabout, John W.	Rochester
‡	Beahrs, Oliver H.	Rochester
†	Beaudry, Rene'	Rochester
†	Beaumier, John H.	Rochester
†	Becton, James L.	Rochester
‡	Belau, Paul G.	Rochester
†	Benedict, William L.	Rochester
‡	Bennett, Clayton J.	Rochester
#	Benson, William F.	Rochester
‡	Berge, Kenneth G.	Rochester
†‡	Berkman, John M.	Rochester
‡	Bernatz, Philip E.	Rochester
‡	Bianco, Anthony J., Jr.	Rochester
‡	Bickel, William H.	Rochester
	Bickford, Joyce A.	Malibu, Calif.
†	Bigelow, Charles E.	Dodge Center
†	Birtwell, William M., Jr.	Rochester
	Bisell, Harry F.	Rochester
‡	Black, B. Marden	Rochester
‡	Blackburn, Charles M.	Rochester
†	Blackwell, Charles W.	Rochester
†	Blair, Thomas R.	Rochester
#	Blodgett, Randolph C., Jr.	Belleville, Illinois
†	Blouin, Yvan P.	Rochester
†	Bolton, Charles F.	Rochester
†	Boseker, Edward H.	Rochester
†	Botting, Arthur J.	Rochester
‡	Bowie, E. J. Walter	Rochester
‡	Boyd, David A., Jr.	Rochester
†	Braasch, William F.	Rochester
‡	Brandenburg, Robert O.	Rochester
‡	Brannick, Thomas L.	Rochester
	Brattensborg, Henry J.	Rochester
‡	Broadbent, James C.	Rochester
‡	Brodhun, John C.	Rochester
†	Brookler, Kenneth H.	Rochester
†‡	Brown, Alex E.	Bradenton, Florida
‡	Brown, Arnold L.	Rochester
†	Brown, Donald J.	Rochester
‡	Brown, Henry A.	Rochester
	Brown, James A.	Rochester
	Brown, James P.	Ft. Defiance, Arizona
‡	Brown, Joe R.	Rochester
†‡	Brown, Philip W.	Rochester
‡	Brown, Philip W., Jr.	Rochester
‡	Brunsting, Louis A.	Rochester
†	Bryar, George E.	Rochester
†	Buie, Louis A.	Rochester
‡	Burbank, Mahlon K.	Rochester
‡	Burchell, Howard B.	Rochester
‡	Burgert, E. O., Jr.	Rochester
	Burgess, Glenn N.	Rochester
‡	Burich, Harry F.	Rochester
‡	Burke, Edmund C.	Rochester
†	Burkhart, J. MacDonald	Baltimore, Maryland
	Burstein, Stephen D.	Rochester
‡	Burton, Robert C.	Rochester
†	Buscemi, Michael F.	Rochester
†	Butsch, John L.	Rochester
‡	Butt, Hugh R.	Rochester
‡	Cain, James C.	Rochester
‡	Callahan, John A.	Rochester
‡	Campbell, Donald C.	Rochester
‡	Campbell, Malcolm K.	Rochester
‡	Carlson, Harley C.	Rochester
	Carr, David T.	Rochester
‡	Carryer, Haddon M.	Rochester
‡	Carter, Earl T.	Rochester

Zumbro Valley Medical Society (Continued)

†	Carter, James B.	Rochester
†	Cassella, Robert R.	Rochester
	Castillo, Richard L.	Plainview
†	Cerino, Lawrence E.	Rochester
†	Cheskes, Albert	Rochester
†	Chesnut, John K.	Oklahoma City, Oklahoma
‡	Childs, Donald S., Jr.	Rochester
‡	Christensen, Norman A.	Rochester
	Cicciarelli, Francis E.	Peoria, Illinois
‡	Clagett, O. Theron	Rochester
†	Clark, Edward C.	Rochester
†	Clark, Leslie W.	Manchester, Iowa
†	Clifton, Theodore A.	Hollywood, Florida
	Coburn, William M., Jr.	Phoenix, Ariz.
†	Coder, Donald M.	Rochester
‡	Cody, D. Thane	Rochester
	Cohen, David F.	London, England
‡	Colby, Malcolm Y., Jr.	Rochester
‡	Coles, Douglas T.	Rochester
†	Colligan, Paul C.	Rochester
	Colton, Roger S.	Rochester
†	Comer, Thomas P.	Rochester
‡	Connolly, Daniel C.	Rochester
‡	Cook, Edward N.	Rochester
‡	Cooper, Talbert	Rochester
‡	Corbin, Kendall B.	Rochester
†	Corcoran, James R.	Rochester
‡	Corrigan, Cyril J.	Rochester
‡	Coventry, Markham B.	Rochester
#	Crandall, Earle E.	San Diego, California
†	Crowder, Bennett L., II	Rochester
	Crusinberry, Charles S.	Des Moines, Iowa
‡	Culp, Clyde E.	Rochester
‡	Culp, Ormond S	Rochester
†	Cummins, Ben M.	Rochester
	Cupps, Roger E.	Rochester
†	Cyrowski, Gerald A.	Rochester
‡	Dahlin, David C.	Rochester
	Dale, Allan J. D.	Rochester
†	Dally, Alfred D.	Rochester
‡	Daugherty, Guy W.	Rochester
†‡	Davidson, Allan D.	Rochester
†	Davidson, Horace B., Jr.	Rochester
†	Davignon, Jean	New York, New York
†	Davis, Austin C.	Pompano Beach, Florida
‡	Davis, George D.	Rochester
‡	Dearing, William H.	Rochester
‡	Decker, David G.	Rochester
†	Dega, Francis J.	Rochester
†	De Mordaunt, Paul R.	Rochester
†	De Remee, Richard A.	Rochester
†	De Santo, Lawrence W.	Rochester
‡	Devine, Kenneth D.	Rochester
	Devloo, Robert A.	Rochester
‡	DeWeerd, James H.	Rochester
‡	Dickson, Edgar R.	Rochester
‡	Didier, Edward P.	Rochester
‡	Diessner, Grant R.	Rochester
#	Dietrich, Robert A.	Augusta, Ga.
	Dillman, Carl E., Jr	Rochester
‡	Dinapoli, Robert P.	Rochester
‡	Dines, David E.	Rochester
‡	Divertie, Matthew B.	Rochester
†	Dixon, Claude F.	Rochester
‡	Dockerty, Malcolm B.	Rochester
†	Donadio, James V., Jr.	Rochester
‡	Donoghue, Francis E.	Rochester
†	Douglas, William W.	Rochester
‡	Douglass, Bruce E.	Rochester
‡	Dower, John C.	Rochester
‡	Doyle, James R.	Rochester
†‡	Drexler, Charles J.	Rochester
†	Drips, Della G.	Rochester
	Druffner, Charles R.	Rochester
	Dubnow, Morton H.	Rochester
‡	Du Shane, James W.	Rochester
#	Duval, David L.	Patuxent River, Maryland
†	Duvoisin, George E.	Rochester
‡	Dyck, Peter J.	Rochester
‡	Dyer, John A.	Rochester
†	Eckman, Philip L.	Rochester
†	Edwards Walter G., Jr.	Rochester
	Eichel, Berkley S.	Rochester
†	Eichler, George R.	Rochester
‡	Elkins, Earl C.	Rochester
‡	Ellis, F. Henry, Jr.	Rochester
‡	Emmett, John L.	Rochester
†	Emmons, Helen J.	Rochester
‡	Emslander, Richard F.	Rochester
‡	Engel, Andrew G.	Rochester
	Engels, Edward P.	Rochester
‡	Erich, John B.	Rochester
‡	Erickson, Donald J.	Rochester
‡	Espinosa, Raul	Rochester
†‡	Eusterman, George B.	Rochester
†	Eusterman, James N.	San Francisco, Calif.
†	Evans, William B.	Rochester
†	Evarts, Arrah B.	Rochester
‡	Faber, John E.	Rochester
†	Fabi, Robert A.	Rochester
‡	Fairbairn, John F.	Rochester
†	Farrow, George M.	Rochester
‡	Faulconer, Albert, Jr.	Rochester
†	Fawcett, Kenneth J.	Rochester
†	Feinberg, Jack H.	Rochester
	Feldmann, Floyd M.	New York, N. Y.
†	Feldt, Robert H.	Rochester
†	Felsoory, Attila	Rochester
‡	Ferguson, Richard H.	Rochester
†	Fernandez, Rafael	Rochester
‡	Ferris, Deward O.	Rochester
	Fiedler, Richard J.	Rochester
‡	Field, Charles A.	Rochester
†‡	Figi, Frederick A.	Rochester
†	Finkelstein, Joel	Rochester
#	Finley, Thomas V.	Glasgow, AFB, Montana
†	Fishman, Norton L.	Rochester
‡	Fluegel, John O.	Rochester
†	Foley, Ralph B.	Rochester
‡	Fontana, Robert S.	Rochester
†	Forth, Ronald J.	Rochester
	Foss, Edward L.	Rochester
‡	Foulk, William T., Jr.	Rochester
#	Francis, Robert L.	Fullerton, Calif.
†	Freeman, F. Julian	Rochester
‡	Frethem, Allen A.	Rochester
†	Fricke, Robert E.	Rochester
#	Friedman, Laurence L.	San Francisco, California
†	Fuller, Alen M.	Rochester
	Fuller, Henry, Jr.	Rochester
†	Furlow, William L.	Rochester
†	Gaines, Richard K.	Rochester

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Zumbro Valley Medical Society (Continued)

	Galloway, Jackson R.	Alexandria, La.
†‡	Gambill, Carl M.	Rochester
‡	Gambill, Earl E.	Rochester
†	Gambill, Harold D.	Rochester
†	Garber, James J.	Rochester
†	Garrick, James G.	Rochester
†	Gasior, Robert M.	Rochester
†	Gasman, David H.	Rochester
#	Gasser, Richard C.	Witchita Falls, Texas
‡	Gastineau, Clifford F.	Rochester
‡	Gedge, Stafford W.	Rochester
#	Gelety, Joseph E.	Lackland, AFB, Texas
‡	Geraci, Joseph E.	Rochester
†	Geurkink, Nathan A.	Rochester
†	Giffin, Herbert Z.	Rochester
†	Gilbaugh, James H., Jr.	Rochester
†	Gilchrist, Ronald W., Jr.	Rochester
	Gillis, Samuel P.	Rochester
†	Giroux, Jean-Mario	Montreal, Canada
†	Gisvold, John J.	Rochester
	Glazer, Ira M.	Rochester
	Glick, Dallas D.	Mountain Lake
‡	Goldstein, Norman P.	Rochester
‡	Goldston, Edgar C.	Rochester
‡	Good, C. Allen, Jr.	Rochester
†	Gordon, Michael S.	Rochester
†	Gordon, Richard S.	Rochester
‡	Gould, Allan B., Jr.	Rochester
†	Gowan, Lawrence R., Jr.	Rochester
†	Gracey, Douglas R.	Rochester
†	Green, George R.	Rochester
‡	Green, Paul A.	Rochester
†	Greenberg, Eugene	Rochester
†	Greene, Jerry G.	Rochester
‡	Greene, Laurence F.	Rochester
‡	Gregg, James A.	Rochester
†	Grimes, Allen E., Jr.	Rochester
†‡	Grindlay, John H.	Rochester
‡	Gross, John B.	Rochester
†	Guillory, Joel R., Jr.	Rochester
†	Gurtner, Gail H.	Rochester
†	Hacker, Philip K.	Rochester
‡	Hagedorn, Albert B.	Rochester
†	Haidinyak, Anton L.	Rochester
‡	Hahn, Richard G.	Rochester
†‡	Haines, Samuel F.	Rochester
†	Hall, Jack W.	Rochester
‡	Hallberg, Olav E.	Rochester
‡	Hallenbeck, George A.	Rochester
‡	Hanlon, David G.	Rochester
†	Hansen, Raymond L.	Rochester
‡	Hanson, Norbert O.	Rochester
†	Hanton, Edward M.	Rochester
‡	Hargraves, Malcolm	Rochester
†	Harrington, Ryan B.	Rochester
†	Harrington, Stuart W.	Rochester
‡	Harris, Lloyd E.	Rochester
‡	Harrison, Carlos E.	Rochester
‡	Harrison, Edgar G., Jr.	Rochester
	Hartridge, Virginia B.	Rochester
	Harville, Donald D.	Rochester
#	Hauser, Walter H.	Ft. Bragg, No. Carolina
†	Havens, Fred Z.	Rochester
‡	Hayles, Alvin B.	Rochester
†	Hays, James C.	Rochester
†	Heck, Frank J.	Wakefield, N. H.
†‡	Heidel, Werner	Rochester
	Hench, Philip K.	La Jolla, Calif.
†	Henderson, Darrell L.	Rochester
‡	Henderson, Edward D.	Rochester
‡	Henderson, John W.	Rochester
‡	Henderson, Lowell L.	Rochester
‡	Hepper, Norman G.	Rochester
†	Hewitt, Edith S.	Rochester
†	Hewitt, Richard M.	Rochester
‡	Higgins, John A.	Rochester
†	Hilgers, Robert D.	Rochester
‡	Hill, John R.	Rochester
‡	Hill, Richard W.	Rochester
	Hines, Edgar A., Jr.	Brevard, N. C.
‡	Hodgson, Corrin H.	Rochester
‡	Hodgson, John R.	Rochester
‡	Hoffman, Harry N., II	Rochester
	Holbrook, Margaret A.	Rochester
	Holland, C. R.	Rochester
‡	Hollenhorst, Robert W.	Rochester
‡	Holley, Keith E.	Rochester
†	Hollowell, O. Weems	Rochester
‡	Holman, Colin B.	Rochester
‡	Hoover, Norman W.	Rochester
#	Hopkins, Donald M.	Chelsea, Mass.
†	Horner, Bennett A.	Rochester
†	Horner, Frances A.	Rochester
†‡	Horton, Bayard T.	Rochester
†	Houston, Hal E., Jr.	Rochester
‡	Howard, Frank M., Jr.	Rochester
‡	Howell, Llewelyn P.	Rochester
†	Hudgins, Robert L.	Rochester
†	Hughes, Rollin W., Jr.	Philadelphia, Pa.
‡	Huizenga, Kenneth A.	Rochester
‡	Hunder, Gene G.	Rochester
‡	Hunt, Arthur B.	Rochester
‡	Hunt, James C.	Rochester
†	Hutton, Frederick A.	Rochester
‡	Ivins, John C.	Rochester
‡	Ivy, Horace K.	Rochester
‡	Jackman, Raymond J.	Rochester
†	Janes, Donald R.	Rochester
‡	Janes, Joseph M.	Rochester
#	Janis, John F.	Ft. Eustis, Va.
	Jensen, Paul A.	Minneapolis
‡	Johnson, Carl E.	Rochester
†	Johnson, Dexter W.	Rochester
‡	Johnson, Einer, W., Jr.	Rochester
	Johnson, George M.	Rochester
†	Johnson, Gerhard J.	Rochester
	Johnson, L. Morris	Smethport, Pa.
	Johnson, Ralph B.	Lanesboro
†	Johnson, Thomas R.	Rochester
‡	Johnson, Victor	Rochester
	Johnson, Walter K.	New Kensington, Pa.
‡	Johnson, William J.	Rochester
†	Jones, Frank E.	Rochester
†	Jones, Harry F.	Rochester
†	Jones, H. Royden, Jr.	Rochester
‡	Joyce, George L.	Rochester
‡	Joyce, John W.	Rochester

Zumbro Valley Medical Society (Continued)

‡ Judd, Edward S. .... Rochester
‡ Juergens, John L. .... Rochester
‡ Kaese, Werner E. .... Rochester
‡ Karnes, William E. .... Rochester
‡ Kavanaugh, Gerald J. .... Rochester
‡ Kazmier, Francis J. .... Rochester
‡ Kearns, Thomas P. .... Rochester
‡ Keating, F. Raymond .... Rochester
‡ Keith, Haddow M. .... Rochester
† Keith, Norman M. .... Rochester
† Kelley, John J. .... Rochester
‡ Kelly, Patrick J. .... Rochester
‡ Kempers, Roger D. .... Rochester
† Kennedy, Charles C. .... Rochester
†‡ Kennedy, Roger L. J. .... Rochester
†‡ Kernohan, James W. .... Rochester
Kettering, Ronald F. .... Rochester
‡ Kiely, Joseph M. .... Rochester
‡ Kierland, Robert R. .... Rochester
† Kimber, William J. .... Rochester
‡ Kincaid, Owings W. .... Rochester
† King, John N. .... Rochester
‡ Kinney, Vernard R. .... Rochester
‡ Kirby, Thomas J., Jr. .... Rochester
‡ Kirklin, John W. .... Rochester
Klass, Donald W. .... Rochester
† Kline, Richard J. .... Rochester
‡ Knapp, Robert D., Jr. .... Rochester
‡ Knutson, Lewis A. .... Spring Grove
† Koch, Michael F. .... Rochester
‡ Koelsche, Giles A. .... Rochester
‡ Kottke, Bruce A. .... Rochester
† Krueger, Haven C. .... Rochester
‡ Krupp, Neal E. .... Rochester
# Kublin, John G. .... Gallup, New Mexico
‡ Kvale, Walter F. .... Rochester
‡ Kyle, Robert A. .... Rochester
‡ Lake, Clifford F. .... Rochester
† Lapp, N. LeRoy .... Rochester
Larson, Leland .... Rochester
† Larson, Richard E. .... Rochester
† Lawrence, Harry M., Jr. .... Rochester
‡ Layton, Donald D., Jr. .... Rochester
† Lee, John C. .... Rochester
‡ Lee, Robert E. .... Rochester
Lehar, Thomas J. .... Rochester
‡ Leonard, Paul F. .... Rochester
† Lescher, Theodore C. .... Rochester
# Levis, Michael P. .... Wurtsmith A.F.B., Michigan
† Levy, Donald M. .... Rochester
† Lewallen, Gene S. .... Rochester
† Lewis, Andrew J. .... Rochester
† Lewis, Donald L. .... Rochester
‡ Lillie, John C. .... Rochester
# Lindsay, Malcolm L., Jr. .... Fort McClellan, Ala.
‡ Linscheid, Ronald L. .... Rochester
‡ Lipscomb, Paul R. .... Rochester
‡ Litin, Edward M. .... Rochester
‡ Litzow, Thaddeus J. .... Rochester
‡ Lofgren, Eric P. .... Rochester
‡ Lofgren, Karl A. .... Rochester
‡ Logan, George B. .... Rochester
† Long, Richard J. .... Rochester
† Longo, Margaret F. .... Rochester
‡ Love, J. Grafton .... Rochester
† Lowe, Stanley W. .... Rochester

† Lufkin, Murray W. .... Rochester
Lundborg, Richard O. .... Rochester
† Lynch, Andrew C. .... Rochester
† Lynch, Miles W. .... Rochester
‡ Lynn, Hugh B. .... Rochester
† Lysak, Walter R. .... Rochester

‡ McBean, James B. .... Rochester
† McCallister, Ben D. .... Rochester
McCarthy, Laurence .... Rochester
† McCloy, Randolph M. .... Rochester
‡ McConahey, William M., Jr. .... Rochester
McDuffie, Frederic C. .... Rochester
‡ McGill, Douglas B. .... Rochester
‡ McGoon, Dwight C. .... Rochester
‡ McIlrath, Donald C. .... Rochester
McKenna, Charles H. .... Rochester
† McLeod, William A. .... Rochester
‡ McPherson, James R. .... Rochester
# McRoberts, Jerry W. .... Bremerton, Wash.
‡ MacCarty, Collin S. .... Rochester
MacLean, Alexander R. .... Rochester
† Macy, Norman E. .... Rochester
†‡ Magath, Thomas B. .... Rochester
Magid, Gail A. .... Rochester
‡ Maher, Frank T. .... Rochester
† Mair, Douglas D. .... Rochester
‡ Malkasian, George D., Jr. .... Rochester
‡ Mankin, Harold T. .... Rochester
# Manning, Preston C., Jr. .... Columbia, So. Carolina
Marcoux, J. Paul .... Rochester
‡ Martens, Theodore G. .... Rochester
‡ Martin, Gordon M. .... Rochester
‡ Martin, Harold R. .... Rochester
† Martin, John H. .... Rochester
Martin, John K., Jr. .... Rochester
‡ Martin, John T. .... Rochester
‡ Martin, Maurice J. .... Rochester
‡ Martin, William J. .... Rochester
† Masson, Duncan M. .... Rochester
† Masson, James C. .... Rochester
‡ Masson, James K. .... Rochester
† Mastan, Peter F. .... Rochester
‡ Mathieson, Don R. .... Rochester
† Mattson, Donald S. .... Wonju, Korea
† Maupin, Roger A. .... Rochester
Maxwell, James H. .... Colorado Springs, Colo.
† May, John C. .... Elgin, Ill.
Mayne, John G. .... Rochester
†‡ Mayo, Charles W. .... Rochester
† Membery, Joan H. .... Rochester
† Merideth, John .... Rochester
‡ Merritt, Wallace A. .... Rochester
† Meyerding, Henry W. .... Rochester
† Mielke, John E. .... Rochester
† Miller, Alfred .... Rochester
Miller, John W., Jr. .... Rochester
‡ Miller, Roland D. .... Rochester
‡ Miller, Ross, H. .... Rochester
‡ Miller, W. Eugene .... Rochester
‡ Millikan, Clark H. .... Rochester
‡ Mills, Stephen D. .... Rochester
† Moeller, Henry G., IV .... Rochester
†‡ Moersch, Fred P. .... Fort Lauderdale, Florida

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Zumbro Valley Medical Society (Continued)

‡	Moertel, Charles G.	Rochester
‡	Molnar, George D.	Rochester
†‡	Montgomery, Hamilton	Rochester
†	Moore, Gordon L., II	Rochester
	Mori, Hideo	Grand Meadow
‡	Morlock, Carl G.	Rochester
‡	Morrow, George W., Jr.	Rochester
†	Morse, Robert M.	Rochester
‡	Mulder, Donald W.	Rochester
‡	Muller, Sigfrid A.	Rochester
†	Mundy, Betty Lee	Rochester
#	Murray, James J., Jr.	Rochester
	Mussey, Mary E.	Rochester
‡	Myers, Thomas T.	Rochester

†	Nadeau, Claude	Rochester
‡	Neault, Roger W.	Rochester
†	Nelson, Evan L., Jr.	Rochester
†	Nelson, J. Phillip	Rochester
†	Newcomer, Albert D.	Rochester
	Newton, St. Elmo, III	Seattle, Wash.
‡	Nichols, Donald R.	Rochester
†	Nilsen, John A.	Rochester
#	Nirschl, Robert P.	Long Island, New York
†	Nolan, Alfred C.	Minneapolis

	O'Connell, Edward J.	Rochester
†	O'Donnell, Kevin T.	Rochester
†	Oberstein, Barry J.	Rochester
†	Obetz, Samuel W.	Rochester
†	Oels, Helen C.	Rochester
	Olafson, Richard A.	Fargo, N. D.
‡	Olsen, Arthur M.	Rochester
‡	Olson, Ernest A.	Pine Island
	Olson, Grant E.	West Concord
‡	Ongley, Patrick A.	Rochester
#	Onofrio, Burton M.	Chevy Chase, Md.
‡	Onsgard, L. Kenneth	Houston
†	Onstad, Gerald R.	Rochester
	Opitz, Joachim L.	Rochester
‡	Osmundson, Philip J.	Rochester
†	Overby, Philip G.	Rochester
‡	Owen, Charles A., Jr.	Rochester

†	Parkovich, Milan J.	Rochester
‡	Palumbo, Pasquale J.	Rochester
†	Pappas, George	Rochester
‡	Paris, Jaime	Rochester
†	Parker, Joseph C., Jr.	Rochester
‡	Parker, Robert L.	Rochester
	Parkhill, Edith M.	Rochester
‡	Parkin, Thomas W.	Rochester
†	Parsons, William R.	Rochester
‡	Paulson, John A.	Rochester
†	Payne, Stanley R.	Rochester
‡	Payne, W. Spencer	Rochester
†	Peacock, William F., III	Rochester
†	Pearson, John E.	Rochester
	Pease, Gertrude L.	Rochester
†	Peck, Donald A.	Pittsburgh, Pa.
†	Pedace, Francis J.	Rochester
†‡	Pemberton, John deJ	Rochester
†	Pequegnat, Edouarde P.	Rochester
‡	Perry, Harold	Rochester
#	Perry, Hugh, Jr.	A.P.O. New York, New York
‡	Peters, Gustavus A.	Rochester
†	Peterson, Hamlet A.	Rochester
	Peterson, Herbert W.	Rochester
†	Peterson, Lowell F. A.	Rochester
#	Peterson, Richard A.	Seattle, Wash.
†	Peyton, Thomas D.	Rochester
‡	Pilling, Loran F.	Rochester
	Pinell, (Midence), Octavio C.	Rochester
†	Pluth, James R.	Rochester
‡	Polley, Howard F.	Rochester
‡	Pool, T. Lloyd	Rochester
†	Potter, Myron T., II	Rochester
†	Powers, Donald W.	Rochester
‡	Pratt, Joseph H., Jr.	Rochester
‡	Priestley, James T.	Rochester
‡	Pugh, David G.	Rochester
‡	Pulec, Jack L.	Rochester
‡	Purnell, Don C.	Rochester

‡	Ralston, Donald E.	Rochester
†‡	Randall, Lawrence M.	Rochester
‡	Randall, Raymond V.	Rochester
	Raphael, Hugh A.	Rochester
†	Rawls, William E.	Houston, Texas
†	Reed, John H., Jr.	Rochester
†	Reed, Ralph R.	Rochester
†	Reeves, Bradford F.	Rochester
	Reiher, Jean	Rochester
‡	Reitemeier, Richard J.	Rochester
‡	Re Mine, William H., Jr.	Rochester
‡	Restall, Charles J.	Rochester
†	Rheault, J. Gerald	Rochester
†	Rhodes, Rollie E., Jr.	Rochester
‡	Riggs, Byron L., Jr.	Rochester
†	Riley, Fenwick, C.	Rochester
‡	Risser, Alden F.	Stewartville
‡	Ritter, Donald G.	Rochester
†	Robertson, Dennis M.	Rochester
‡	Rogne, William G.	Spring Grove
‡	Rome, Howard P.	Rochester
‡	Rooke, Edward D.	Rochester
†	Rosenow, Edward C., III	Rochester
‡	Rosevear, John W.	Rochester
‡	Ross, James V., Jr.	Rochester
	Roth, Sanford H.	Rochester
‡	Rovelstad, Randolph A.	Rochester
†	Rubinstein, Mark M.	Rochester
‡	Rucker, Charles W.	Rochester
#	Rudis, Bernard P.	Fort Knox, Kentucky
‡	Rushton, Joseph G.	Rochester
†	Russell, Thomas J.	Rochester
‡	Rynearson, Edward H.	Rochester
	Rynearson, Robert R.	Rochester

†	Sakulsky, Stephen B.	Rochester
‡	Salassa, Robert M.	Rochester
‡	Sander, Frank V., Jr.	Rochester
#	Sanders, William M.	Montgomery, Ala.
‡	Sanderson, David R.	Rochester
†	Sandow, Theodore L., Jr.	Rochester
‡	Sauer, William G.	Rochester
†	Sawtell, Robert R.	Rochester
	Sayre, George P.	Rochester
‡	Scanlon, Paul W.	Rochester
	Schattenberg, Thomas T.	Rochester
	Schirger, Alexander	Rochester
†	Schmid, Walter C.	Rochester
†	Schnell, Roger G.	Rochester
‡	Schoenfield, Leslie J.	Stockholm, Sweden
‡	Scholz, Donald A.	Rochester
†	Schreiner, Betty J.	Rochester

Zumbro Valley Medical Society (Continued)

†	Schulze, Robert R.	Rochester
	Schutt, Allan J.	Rochester
	Schutt, Ann H.	Rochester
‡	Scudamore, Harold H.	Rochester
‡	Sedlack, Richard E.	Rochester
‡	Seldon, Thomas H.	Rochester
#	Senft, Robert A.	Mountain Home AFB, Idaho
‡	Sessler, Alan D.	Rochester
#	Shamblin, James R., Jr.	Columbus, Georgia
#	Sheldon, Richard S.	Ft. Hood, Texas
‡	Sheps, Sheldon G.	Rochester
‡	Shick, Richard M.	Rochester
†	Sickels, William F.	Rochester
‡	Siekert, Robert G.	Rochester
†	Sigler, Robert M.	Rochester
†	Silverberg, Donald S.	Rochester
†	Silverman, Louis F.	Rochester
‡	Silverstein, Murray N.	Rochester
‡	Simonton, Kinsey M.	Rochester
‡	Skaug, Harold M.	Chatfield
‡	Slocumb, Charles H.	Rochester
#	Smith, David E.	Ft. Knox, Ky.
†	Smith, David L.	Rochester
†	Smith, Frederick L.	Rochester
†	Smith, George R.	Rochester
†	Smith, Harry L.	Rochester
‡	Smith, Lucian A.	Rochester
‡	Smith, Ralph E.	Rochester
‡	Smith, Reginald A.	Rochester
	Smith, Richard D.	Rochester
†	Smith, Robert J., Jr.	Rochester
‡	Sones, Donald A.	Rochester
‡	Soule, Edward H.	Rochester
	Spackman, Fred N.	Rochester
‡	Spencer, Robert J.	Rochester
‡	Spiekerman, Ralph E.	Rochester
‡	Spittell, John A., Jr.	Rochester
‡	Sprague, Randall G.	Rochester
	Stack, Robert E.	Rochester
†	Stackhouse (Smith) Ethel M.	Rochester
‡	Stauffer, Maurice H.	Rochester
†	Stayura, Lois A.	Rochester
†	Stecker, Raymond H.	Rochester
†	Stein, Ronald B.	Encino, Calif.
‡	Steinhilber, Richard M.	Rochester
‡	Stewart, James R.	Rochester
‡	Stickney, J. M.	Rochester
‡	Stillwell, George K.	Rochester
‡	Stilwell, George G.	Rochester
#	Stobbe, Juergen A.	New York, New York
	Stobbe, Knud C.	Rochester
	Striebel, James L.	Brookline, Mass.
‡	Stroebel, Charles F., Jr.	Rochester
†	Strong, Cameron G.	Montreal, Canada
†	Stuart, Frank A., III	Rochester
‡	Sullivan, Charles R.	Rochester
‡	Summerskill, William H.	Rochester
‡	Svien, Hendrik J.	Rochester
‡	Swedlund, Harry A.	Rochester
‡	Symmonds, Richard E.	Rochester
	Tager, Michael G.	Rochester
‡	Taswell, Howard F.	Rochester
‡	Tauxe, Welby N.	Rochester
†	Teller, Richard M.	Rochester
†	Templeton, Mary J.	Rochester
	Thomas, Juergen E.	Rochester
†	Thomas, Russell L.	Rochester
†	Thomford, Neil R.	Rochester
†	Thompson, Dennis P.	Rochester
‡	Thompson, Gershom J.	Rochester
†	Thompson, Gershom J., Jr.	Rochester
	Thompson, James P., Jr.	Rochester
†	Thorson, Stephen C.	Rochester
‡	Thurber, Deloran L.	Rochester
‡	Tillisch, Jan H.	Rochester
†	Tillman, Billups P.	Rochester
‡	Tinkham, Robert G.	Rochester
‡	Titus, Jack L.	Rochester
†	Todd, David W.	Rochester
†	Tomori, William Y.	Rochester
#	Tsang, Donald	San Francisco, California
	Tsang, Lenore A.	Monterey, Calif.
#	Turner, Norman S.	Gallup, New Mexico
	Tyce, Francis A.	Rochester
‡	Uihlein, Alfred	Rochester
‡	Underdahl, Laurentius O.	Rochester
‡	Utz, David C.	Rochester
	Utz, Philip H.	La Crescent
‡	Van Herik, Martin	Rochester
†	Van Wie, August E.	Rochester
‡	Vaughn, Louis D.	Rochester
	Veneziale, Carlo M.	Rochester
‡	Verby, John E.	Rochester
†	Vesper, Lee J.	Rochester
	Virnig, Hildegard J.	Caledonia
†	Von Gemmingen, George R.	Rochester
†	Vrabec, Donald P.	Rochester
‡	Wagoner, Richard D.	Rochester
†	Wahman, Robert E.	Rochester
†	Wakim, Khalil G.	Rochester
‡	Wallace, Robert B.	Rochester
†	Walls, Joseph T.	Rochester
†	Walsh, John G.	Rochester
†	Walsh, John H.	Rochester
†‡	Walters, Waltman	Rochester
‡	Waltz, Arthur G.	Rochester
‡	Ward, Louis E.	Rochester
†	Warner, Robert C.	Rochester
†	Waterhouse, Blake E.	Rochester
†‡	Watkins, Charles H.	Redlands, Calif.
†	Weaver, Arthur L.	Rochester
†	Webb, Donald E.	Rochester
‡	Weed, Lyle A.	Rochester
‡	Weeks, Richard E.	Rochester
‡	Weidman, William H.	Rochester
†	Weingart, Jon L.	Rochester
†	Weinman, Darrell T.	Rochester
†‡	Weir, James F.	Rochester
†	Weis, Andrew J.	Rochester
‡	Welch, John S.	Rochester
‡	Wellman, William E.	Rochester
	Wellner, Theodore O.	Rochester
‡	Wente, Harold A.	Rochester
	Westrup, John E.	Lanesboro
†	Wheeler, Donald K.	Rochester
‡	Whisnant, Jack P.	Rochester
	Whisnant, Robert A., Jr.	Rochester
†	Whitaker, John J.	San Antonio, Texas
†	White, William L.	Rochester
†	Whittaker, Lorin D., Jr.	Rochester
	Wiederholt, Wigbert C.	Rochester
†	Wilbur, Robert D.	Rochester

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Zumbro Valley Medical Society (Continued)

†	Wilkowske, Conrad J.	Rochester
†	Williams, David Earle	Rochester
#	Williams, David Eugene	Lahore, W. Pakistan
‡	Williams, Tiffany J.	Rochester
†	Willius, Fredrick A.	Rochester
†	Wilson, M. Robert	Rochester
‡	Wilson, Robert B.	Rochester
‡	Wilson, Viktor O.	Rochester
†	Wiltsie, John C.	Rochester
‡	Winkelmann, Richard K.	Rochester
‡	Witten, David M.	Rochester
‡	Wollaeger, Eric E.	Rochester
*†	Woltman, Henry W.	Rochester
†	Wood, Lloyd T.	Rochester
†	Woods, John E.	Rochester
†	Woolam, Gerald L.	Rochester
‡	Woolner, Lewis B.	Rochester
‡	Worthington, John W., Jr.	Rochester
†	Wright, Charles L., Jr.	Rochester
†	Wychulis, Adam R.	Rochester
†	Wyckoff, Francis J.	Rochester
†	Wyman, John B.	Rochester
†	Yalowitz, Philip A.	Rochester
‡	Yoss, Robert E.	Rochester
‡	Young, Henry H.	Rochester
	Yudell, Alan	Rochester
†	Zacharski, Leo R.	Rochester

ALPHABETIC ROSTER

Key to Symbols

# Service
* Deceased
† Life, Associate, Affiliate and Resident
¶ Honorary

A

†	Aanes, Almer M.	Red Wing
	Aaro, Leonard A.	Rochester
	Abraham, Arden L.	Duluth
	Abrams, Alexander, Jr.	St. Paul
	Abramson, Burton I.	Minneapolis
	Abramson, Milton	Minneapolis
	Abullarade, Jose A.	Minneapolis
	Adair, Albert F., Jr.	St. Paul
	Adams, Harold R.	St. Paul
	Adams, Patrick J.	Shakopee
	Adcock, Leon L.	Minneapolis
	Addy, Edward R.	Gilbert
	Adkins, C. Douglas	Minneapolis
	Adkins, Galen H.	Cambridge
	Adkins, James T.	Bertha
	Adson, Martin A.	Rochester
	Adler, Franz A.	Rochester
	Affeldt, Daniel E.	Kasson
	Aga, John H.	Brainerd
	Agustsson, Hreidar	Minneapolis
	Ahern, Eugene E.	Minneapolis
†	Ahlfs, Jacob J.	Minnetonka
	Ahlstrom, Robert C.	Braham
†	Ahmann, David L.	Rochester
	Ahola, Kenneth E.	Hibbing
	Ahrens, Curtis F.	Duluth
	Ahrens, Robert M.	St. Paul
	Akins, Willard M.	Red Wing
	Alari, Heino	Minneapolis
	Albrecht, Raymond J.	St. Paul
	Alcorn, William J.	Wabasso
	Alden, Charles W.	Kimball
	Alden, John F.	St. Paul
†	Aldrete, Joaquin S.	Rochester
	Alexander, Harlan A.	Minneapolis
	Aling, Charles A.	Minneapolis
#	Allen, Charles V.	Modesto, Calif.
	Allen, James R.	Edina
	Allen, John H.	Montevideo
	Allison, David D.	Litchfield
†	Allocco, Dominic J.	Rochester
	Alter, Milton	Minneapolis
†	Altnow, Hugo O.	Coral Gables, Florida
	Alton, Donald G.	St. Paul
	Amatuzio, Donald S.	Minneapolis
†	Amberg, Samuel	Rochester
	Amerongen, Werner W.	St. Paul
	Amick, Arthur	Worthington
	Amren, Don P.	Minneapolis
#	Amundsen, Melvin A.	Denver, Colo.
	Anderegg, Alfred F.	St. Paul
	Andersen, Howard A.	Rochester
	Andersen, James G.	Minneapolis
†	Andersen, Robert L.	Rochester
	Anderson, Arden O.	Brainerd
	Anderson, Arnold S.	Minneapolis
	Anderson, Ben H.	Minneapolis
	Anderson, Chester A.	Hector
	Anderson, Chester A.	Madison
†	Anderson, Dale L.	Rochester
	Anderson, David M.	Minneapolis
	Anderson, David P., Jr.	Austin
†	Anderson, Edward D.	Vaud, Switzerland
	Anderson, Ernest R.	Minneapolis
	Anderson, Frank J.	Minneapolis
	Anderson, Franklin	Owatonna
	Anderson, Harold J.	Austin
	Anderson, James J.	St. Paul
	Anderson, Jo E.	LeSueur
	Anderson, John A.	Minneapolis
	Anderson, John W.	Blue Earth
	Anderson, Karl W.	Minneapolis
	Anderson, Margaret C.	St. Paul
†	Anderson, Mark J.	Rochester
	Anderson, Markham J., Jr.	Rochester
	Anderson, Milton W.	Rochester
	Anderson, Oscar D.	Mankato
†	Anderson, Richard E.	Willmar
†	Anderson, Richard W.	St. Paul
	Anderson, Richard W.	Minneapolis
	Anderson, Roger E.	Minneapolis
	Anderson, Roger L.	Minneapolis
	Anderson, Roland G.	Thief River Falls
	Anderson, Russell H.	Virginia
	Anderson, Thomas P.	Minneapolis
	Anderson, U. Schuyler	Fargo, No. Dakota
	Anderson, Waldo P.	Buffalo
	Anderson, Wallace E.	Clearbrook
	Anderson, Wallace E.	Minneapolis
	Anderson, Wallace R.	Minneapolis
	Anderson, Werner W.	Brainerd
	Anderson, William H.	Minneapolis
	Anderson, William T.	Minneapolis
†	Andreassen, Einar C.	Minneapolis
	Andreassen, Rolf L.	Minneapolis
†	Andreini, Paul H.	Rochester
	Andresen, Karl d'A	Minneapolis
†	Angros, Richard H.	Rochester
	Ankner, Frank J.	Minneapolis
	Anonsen, Richard E.	Minneapolis
†	Anquist, Kenneth A.	Rochester
	Anselment, Lois A.	Excelsior
	Antonow, Arthur M.	Virginia
†	Anzalotta-Hernandez, Jose	Rochester
	Appleman, Robert M.	Rochester
	Archambeau, Paul L.	Sebastopol, California
†	Arends, Archabald L.	Minneapolis
	Arey, Stuart Lane	Minneapolis
	Arhelger, Stuart W.	Minneapolis
	Arlander, Clarence E.	Minneapolis
	Arling, Leonard S.	Minneapolis
	Arms, James J.	Minneapolis
	Armstrong, Byron H.	Minneapolis
	Armstrong, Ralph S.	Winnebago
†	Arndt, Harry W.	Detroit Lakes
	Arnesen, John F.	Owatonna
	Arnesen, Paul M.	Mankato
	Arneson, Arthur I.	Morris
	Arnold, Ann W.	Minneapolis
	Arnold, Arthur L.	Albert Lea
†	Arnold, Gordon B.	Rochester
	Arnold, Thomas B.	Minneapolis

*	Arnquist, Andrew S.	St. Paul
	Arny, Frederick P.	St. Paul
†	Arvidson, Carl G.	Minneapolis
	Arzt, Philip K.	St. Paul
	Ashmore, Herbert C.	St. Paul
	Asta, Joseph J.	Duluth
†	Athens, Alvin G.	Santa Barbara, California
	Atmore, William G.	Duluth
†	Atwood, Roger M.	Rochester

	Aufderheide, Arthur C.	Duluth
†	Auger, Armand J.	Rochester
	Aughenbaugh, John W.	Minneapolis
	Aulick, Ernest J.	Paynesville
	Aurelius, J. Richards	St. Paul
	Ausman, Duane R.	St. Paul
	Austrian, Sol	St. Paul
	Autrey, William A.	St. Cloud
	Azad, A. M.	Minneapolis

B

	Baab, Robert O.	Crookston
	Baars, Conrad W.	Rochester
	Babb, Frank S.	St. Paul
†	Babb, Richard R.	Rochester
	Bach, Jerome	St. Paul
	Backus, Byron C.	Cloquet
	Backus, Lloyd B.	Cloquet
	Backus, Reno W.	Nopeming
†	Badeaux, George I.	Brainerd
	Bader, J. L.	Slayton
	Baggenstoss, Archie H.	Rochester
	Baggenstoss, Osmond J.	Minneapolis
	Bagley, Charles M.	Duluth
	Bagley, Elizabeth C.	Duluth
	Bagley, Russell W.	Minneapolis
†	Bagley, William R.	Duluth
	Bah, Merle C.	St. Paul
	Baich, Velemir M.	Coleraine
	Bair, Hugo L.	Rochester
	Baird, Raymond L.	Harmony
†	Baitz, Thomas	Rochester
¶	Bajec, Dusan	Poljane, Yugoslavia
	Baken, Melvin P.	Minneapolis
	Baken, Melvin P., Jr.	Minneapolis
	Baker, Abe B.	Minneapolis
†	Baker, Alfred T.	Minneapolis
	Baker, C. Camak	Minneapolis
	Baker, Chilton R., Jr.	St. Paul
	Baker, George S.	Rochester
†	Baker, Harry R.	Hayfield
	Baker, Hillier L., Jr.	Rochester
†	Baker, James A.	Rochester
	Baker, Jeannette L.	Fergus Falls
	Baker, Milton E.	Minneapolis
	Baker, Norman H.	Fergus Falls
	Bakke, Arnold C.	Minneapolis
	Bakkila, Henry E.	Duluth
	Balce, Regino V.	St. Paul
*	Balcome, Milton M.	St. Paul
	Baleisis, Peter	Minneapolis
	Balfour, William M.	Lawrence, Kansas
	Balkin, Samuel G.	Minneapolis
	Ballantine, Jerome J.	St. Cloud
	Balmer, Albert I.	Duluth
	Balogh, Charles J.	Minneapolis
†	Banaszak, Edward F.	Rochester
#	Banitt, Louis W.	A.P.O., New York, New York
	Bank, Harry E.	Minneapolis
	Banner, Edward A.	Rochester
#	Barber, Kent, Jr.	A.P.O. New York, New York
	Barber, Tracy E.	Austin
†	Bard, James W.	Rochester
	Bardon, Richard	Duluth
	Barker, John D.	Duluth
†	Barker, Nelson W.	Rochester

†	Barnes, Arlie R.	Rochester
	Barnes, Richard E.	Aurora
	Barnett, Arthur J.	Foley
	Barnett, Joseph M.	St. Paul
	Barnett, Robert M.	Minneapolis
†	Barney, Leon A.	Duluth
	Barno, Alex	Minneapolis
	Barr, James S.	New York, New York
	Barr, Lowell, C.	Albert Lea
	Barr, Lowell W.	Albert Lea
	Barr, Maxwell M.	Minneapolis
	Barr, Robert N.	Minneapolis
	Barrett, Earl E.	Duluth
	Barrett, Patrick J.	Minneapolis
	Barron, Jesse J.	Minneapolis
†	Barron, Moses	Beverly Hills, California
	Barry, Maurice J., Jr.	Rochester
†	Barsness, Nellie O. N.	St. Paul
	Bartholomew, Lloyd G.	Rochester
	Bartness, John E.	Albert Lea
	Bartzen, Peter J.	Duluth
	Basinger, Harold P.	Windom
	Basinger, Homer P.	Windom
	Bastron, James A.	Rochester
	Bateman, Clarence V.	Fergus Falls
	Batdorf, B. Niles	Mankato
	Bauer, Eugene L.	St. Paul
	Bauer, Paul G.	Faribault
	Baumgartner, Florian H.	Albany
	Bayley, E. Covell	Lake City
	Bayrd, Edwin D.	Rochester
	Beabout, John W.	Rochester
	Beach, Northrop	Minneapolis
	Beahrs, Oliver H.	Rochester
	Bealka, Neil M.	Stillwater
	Bean, Charles N.	Waconia
	Beard, Archibald H., Jr.	Minneapolis
	Beaton, J. Gordon	Northfield
†	Beaudry, Rene	Rochester
†	Beaumier, John H.	Rochester
	Beck, Charles J.	North St. Paul
†	Becker, Arnetta M.	Unknown
	Becker, Kenneth L.	Washington, D. C.
	Becker, Frederic T.	Duluth
	Beckering, Gerrit	Edgerton
	Beckering, Roland G.	Edgerton
†	Becton, James L.	Rochester
	Beek, Harvey O.	St. Paul
	Beer, John J.	St. Paul
†	Behmler, Frederick W.	Morris
	Behr, Orlo K.	Crookston
	Beirstein, Samuel	Minneapolis
	Beiswanger, Richard H.	Minneapolis
	Belau, Paul G.	Rochester
	Belcher, Royden A.	Little Falls

	Bell, Donald C.	Minneapolis
	Bell, Harry M.	Duluth
	Bellomo, James	St. Paul
	Bellomo, John	Fairmont
	Bellville, Titus P.	Minneapolis
	Belz, Reinmar	St. Paul
	Belzer, Meyer S.	Minneapolis
	Bender, James H.	Brainerd
	Bendix, Lester H.	Annandale
†	Benedict, William L.	Rochester
	Benell, Otto E.	Virginia
	Benepe, James L.	St. Paul
	Benesh, Louis A.	Minneapolis
	Benjamin, Edwin G.	Minneapolis
	Benjamin, Harold G.	Minneapolis
	Benjamin, Richard D.	Minneapolis
	Benjamin, Robert B.	Minneapolis
	Benjamin, Walter G.	Pipestone
	Bennett, Clayton J.	Rochester
	Benson, Alfred H.	Little Falls
#	Benson, William F.	Rochester
	Benthack, Elaine M.	Minneapolis
	Bentz. Herman D.	Anoka
	Bepko, Marie K. (Mrs. Puumala)	Cloquet
	Berdez, George L.	Duluth
	Berg, Arnold M.	Roseau
	Berg, Clinton C.	Excelsior
†	Bergan, Otto	Clinton
	Bergan, Robert O.	Duluth
	Berge, Harry L.	Mora
	Berge, Kenneth G.	Rochester
	Berger, Alex G.	Minneapolis
	Berger, Phil R.	St. Cloud
	Bergeron, Dale A.	Le Sueur
	Bergh, George S.	Minneapolis
	Bergh, Solveig M.	Minneapolis
	Berglund, Alvin E.	Cambridge
	Berglund, Eldon B.	Minneapolis
	Bergman, Oscar B.	St. James
	Bergquist, James R.	Minneapolis
†	Berkman, John M.	Rochester
	Berkwitz, Nathaniel J.	Minneapolis
	Berman, David A.	Minneapolis
	Berman, Reuben	Minneapolis
	Bernatz, Philip E.	Rochester
	Bernier, Merrill J.	North St. Paul
	Bernstein, Irving C.	Minneapolis
	Bernstein, William C.	St. Paul
	Berris, Harold	Minneapolis
	Berry, Ronald N.	Minneapolis
	Bessesen, Alfred N.	Minneapolis
	Beuning, John B.	St. Cloud
	Bevis, William D.	Minneapolis
	Bianco, Anthony J.	Duluth
	Bianco, Anthony J., Jr.	Rochester
	Bicek, Joseph F.	St. Paul
	Bickel, William H.	Rochester
	Bickford, Joyce A.	Malibu, California
	Bieter, Raymond N.	Minneapolis
†	Bigelow, Charles E.	Dodge Center
	Bigler, Earl E.	Perham
	Bigler, Ivan E.	Perham
	Bilka, Paul J.	Minneapolis
†	Billings, Harry H.	Red Wing
	Binder, Manuel R.	Minneapolis
†	Binet, Henry E.	Grand Rapids
	Bingham, George C.	Bird Island
	Birkemeyer, Eugene J.	Ely
†	Birtwell, William M., Jr.	Rochester
	Bisel, Harry F.	Rochester
	Bissinger, Lester L.	Brainerd
	Bittick, Wilbur H.	Minneapolis
	Bjornson, Robert G. B.	St. Paul
	Black, B. Marden	Rochester
	Black, Earl J.	St. Paul
†	Black. Leo F.	Rochester
	Black, William A.	New Ulm
	Blackard, Clyde E.	Minneapolis
	Blackburn, Charles M.	Rochester
	Blackburn, Henry W., Jr.	St. Paul
	Blackmore, Sidney C.	Biwabik
†	Blackwell, Charles W.	Rochester
	Blackwell, Leonard H.	Hutchinson
†	Blair, Thomas R.	Rochester
	Blake, Allan J.	Hopkins
	Blake, James A.	Hopkins
	Blake, Paul S.	Minneapolis
	Blaw, Michael E.	Minneapolis
	Bloch, Henry S.	Minneapolis
#	Blodgett, Randolph C., Jr.	Belleville, Illinois
	Bloedel, Traugott J.	Osseo
	Blomberg, Robert D.	Minneapolis
	Blomberg, William R.	St. Paul
	Bloom, David	Minneapolis
	Bloom, Joseph	Silver Bay
	Bloom, Norman B.	Minneapolis
†	Blouin, Yuan P.	Rochester
	Blumberg, Henry B.	St. Paul
	Blumenthal, Malcolm N.	Minneapolis
	Blumer, Arlo R.	Albert Lea
	Boardman, Dalmon V.	Winona
†	Bock, Rolland A.	St. Paul
	Bodaski, Albert A.	Tyler
	Boecker, Bernhard	Duluth
	Bofenkamp, Benjamin	Minneapolis
	Bofenkamp, Ferdinand W.	Luverne
	Bohn, Donald G.	Minneapolis
	Boies, Lawrence R.	Minneapolis
	Boline, Clifford A.	Battle Lake
	Bologna, Camillo V.	Moorhead
†	Bolstad, Owen C.	Ft. Snelling
†	Bolton, Charles F.	Rochester
	Bolz, J. Arnold	Grand Rapids
	Boman, Paul G.	Duluth
	Bonello, Frank J.	St. Paul
	Bonner, John L.	Grand Rapids
	Boody, George J., Jr.	Cambridge
	Boone. Ervin S.	Luverne
	Borg, Joseph F.	St. Paul
	Borgerson, Arthur H.	Long Prairie
	Borman, Chauncey N.	Minneapolis
	Borowicz, Leonard A.	Minneapolis
†	Boseker, Edward H.	Rochester
	Bosland, Howard G.	Willmar
†	Botting, Arthur J.	Rochester
†	Bottolfson, B. T.	Moorhead
†	Bouma, Lewis R.	St. Paul
	Bouquet, Bertram J.	Wabasha
	Bouthilet, Florence J.	Minneapolis
	Bowen, Robert L.	Hibbing
	Bowers. Gordon G.	Minneapolis
	Bowers, Robert N.	Lake City
	Bowie, E. J. Walter	Rochester
	Bowlin, Paul F.	Minneapolis
	Boyd, David A., Jr.	Rochester
	Boyd, Frank E.	Pipestone
	Boyer, Samuel H.	Duluth
	Boyle, Francis J.	Springfield

†	Boynton, Ruth E.	Miami, Florida
	Boysen, Herbert	Madelia
	Boyum, Allan J.	Marshall
	Bozanich, Milosh S.	St. Cloud
†	Braasch, William F.	Rochester
	Brabec, Paul F.	Hastings
	Brace, Ray I.	Clinton
	Bradley, Jeanne B.	Minneapolis
	Bradley, John G.	Minneapolis
	Brainard, John B.	St. Paul
†	Brand, William A.	Redwood Falls
	Brandenburg, Robert O.	Rochester
	Brandt, Henry E.	Minneapolis
†	Branham, Donald S.	Deer Park, Wisconsin
	Brannick, Thomas L.	Rochester
	Bransford, Paul W.	Minneapolis
	Bratholdt, James W.	Watertown
†	Bratrud, Arthur F.	Minneapolis
†	Bratrud, Edward	Alexandria
†	Bratrude, Earl J.	St. James
	Brattensborg, Henry J.	Rochester
	Braun, Ohrmundt C.	Grand Rapids
	Braun, Rene	Minneapolis
	Brauti, E. Fred	Minneapolis
†	Bray, Elwyn R.	St. Paul
	Bray, Philip N.	Duluth
	Breitenbucher, Robert B.	Minneapolis
	Brekke, Harvey J.	Minneapolis
	Brenk, Paul E.	Detroit Lakes
	Brennan, Joseph G.	Minneapolis
	Bretzke, Carl O.	Hutchinson
	Briggs, John F.	St. Paul
	Briggs, Thomas G.	White Bear Lake
	Brigham, Charles F., Jr.	St. Cloud
	Brill, Alice K.	Minneapolis
	Brink, Adlai A.	Baudette
	Brink, Donald M.	St. Peter
	Broadbent, James C.	Rochester
	Broadie, Thomas E.	St. Paul
	Brockway, Roger W.	Grand Rapids
	Brodhun, John C.	Rochester
†	Brodie, Walter D.	St. Paul
	Broker, Henry M.	St. Cloud
	Broman, Harold R., Jr.	North St. Paul
	Brooker, Warren J.	Duluth
†	Brookler, Kenneth H.	Rochester
†	Brooks, Charles N.	Minneapolis
†	Brown, Alex E.	Brandenton, Fla.
	Brown, Arnold L.	Rochester
	Brown, Cyrus C.	Duluth
†	Brown, Donald J.	Rochester
	Brown, Frank T.	St. Cloud
	Brown, Glenn W.	Halstad
	Brown, Hector M.	St. Paul
	Brown, Henry A.	Rochester
	Brown, James A.	Rochester
	Brown, James E., Jr.	St. Paul
	Brown, James P.	Ft. Defiance, Ariz.
	Brown. Joe R.	Rochester
	Brown, John H.	Minneapolis
†	Brown, John M.	Chicago, Ill.
†	Brown, Philip W.	Rochester
	Brown, Philip W., Jr.	Rochester
	Brown, Russell T.	Browerville
	Brown, William D.	Minneapolis
	Brown, William D., Jr.	Minneapolis
	Bruhl, Heinz, H.	Faribault
	Brunsting, Louis A.	Rochester
	Brusegard, James F.	Red Wing
	Bryant, Emmett P.	Ellendale
†	Bryar, George E.	Rochester
	Bucher, Foster D.	Starbuck
	Buchstein, Harold F.	Minneapolis
†	Buck, Frederick H.	Shakopee
	Buckley, Joseph J.	Minneapolis
	Buckley, Robert P.	Duluth
	Buesgens, Ralph H.	Waterville
	Bugenstein, Robert H.	Minneapolis
†	Buie, Louis A.	Rochester
	Buie, Louis A., Jr.	Minneapolis
	Buirge, Raymond E.	Minneapolis
	Bulinski, Theodore J.	St. Paul
	Bundt, Robert E.	Minneapolis
	Bunker, Bevan W.	Anoka
	Burbank, Mahlon K.	Rochester
	Burchell, Howard B.	Rochester
	Buresh, Kenneth L.	Westbrook
	Burgert, E. O., Jr.	Rochester
	Burgess, Glenn N.	Rochester
	Burich, Harry F.	Rochester
	Burke, Edmund C.	Rochester
†	Burkhart, J. MacDonald	Baltimore, Md.
	Burklund, Edwin C.	St. Paul
	Burlingame, David A.	St. Paul
	Burman, Richard E.	Aitkin
	Burmeister, Richard O.	St. Paul
	Burnett, Joseph W.	New Ulm
	Burnham, Wesley H.	Minneapolis
†	Burns, Catherine	Excelsior
	Burns, Floyd M.	Milan
†	Burns, John M.	St. Paul
†	Burns, M. A.	Milan
	Burseth, Edgar C.	Mora
	Burstein, Stephen D.	Rochester
*†	Burton, Carl G.	St. Paul
	Burton, J. Richard	St. Paul
	Burton, Robert C.	Rochester
†	Buscemi, Michael F.	Rochester
†	Buscher, Julius C.	St. Cloud
	Bush, Robert P.	St. Paul
	Bush, Roger A.	Owatonna
	Bushard, Wilford J.	Phoenix, Ariz.
†	Busher, Herbert H.	St. Paul
	Butler, John K.	Cloquet
†	Butsch, John L.	Rochester
	Butt, Hugh R.	Rochester
†	Butturff, Carl R.	Freeborn
†	Butzer, John A.	Mankato
	Butzer, John F.	Mankato
*	Buzzelle, Leonard K.	Minneapolis
	Byrne, William J.	St. Paul

C

	Cable, Morris L.	Minneapolis
	Cabot, Clyde M.	Minneapolis
	Cain, Clark L.	St. Paul
	Cain, James C.	Rochester
	Cain, James H.	Alexandria
	Cairns, Robert J.	Redwood Falls
†	Calhoun, Frank W.	Albert Lea
	Calin, S. Hartley	Minneapolis
	Callahan, John A.	Rochester
†	Cameron, Isabell L.	Minneapolis
	Cameron, John H.	Clovis, New Mexico
	Camp, Ray J.	Madison

†	Campaigne, Robert J.	Minneapolis
	Campbell, Denis V.	Fergus Falls
	Campbell, Donald C.	Rochester
	Campbell, Malcolm K.	Rochester
	Campbell, Orwood J.	Minneapolis
	Campbell, Wayne L.	Waseca
	Canine, James L.	South St. Paul
	Cant, Wilbur F.	Red Wing
†	Cantwell, William F.	International Falls
	Caplan, Leslie	Minneapolis
	Card, William H.	Minneapolis
	Cardle, George E.	Brainerd
	Cardle, James G.	Minneapolis
	Cardle, John B.	Minneapolis
	Carey, James B., Jr.	Minneapolis
	Carey, Lewis S.	St. Paul
	Carlander, Lester W.	Minneapolis
	Carlon, Donald L.	Moorhead
	Carlson, Carl E.	Alexandria
	Carlson, Charles V.	Mound
	Carlson, Harley C.	Rochester
	Carlson, Homer J.	Pelican Rapids
	Carlson. John V.	Westbrook
	Carlson, Lawrence	Minneapolis
	Carlson, Leonard T.	Minneapolis
	Carlson, Lloyd E.	Worthington
	Carlson, Robert G.	Willmar
	Carlson, Russel E.	Stillwater
	Carlson, Vernon J.	Moorhead
	Caron, Robert P.	Minneapolis
	Carr, David T.	Rochester
	Carr, William J.	Minneapolis
	Carroll, John J.	Winsted
	Carryer, Haddon M.	Rochester
	Carter, Donald C.	St. Cloud
	Carter, Earl T.	Rochester
†	Carter, James B.	Rochester
	Carthey, Frank J.	New Ulm
	Caspers, Carl G.	Minneapolis
†	Cassella, Robert R.	Rochester
	Castillo, Richard L.	Plainview
†	Catlin, John J.	Macomb, Ill.
	Catlin, Theodore J.	Buffalo
	Cauble, Charles F.	Minneapolis
†	Cavanor, Frank T.	Minneapolis
	Ceder, Elmer T.	Minneapolis
	Cella, Joseph A.	Minneapolis
	Ceplecha, Stanley F.	Redwood Falls
†	Cerino, Lawrence E.	Rochester
	Cervenka, Charles F.	New Prague
	Cesnik, Robert J.	Sauk Rapids
	Chadbourn, Charles R.	Hudson, Wisconsin
	Chadbourn, Wayne A.	Minneapolis
	Chalgren, William S.	Mankato
	Challman, S. Allan	Minneapolis
	Chandler, William M.	Minneapolis
†	Chatterton, Carl C.	St. Paul
	Chedister, Charles R.	Minneapolis
	Chermak, Francis G.	International Falls
	Chervenak, William A.	Minneapolis
†	Cheskes, Albert	Rochester
	Chesler, Merrill D.	Minneapolis
†	Chesnut, John K.	Oklahoma City, Oklahoma
	Child, Sherman B.	Minneapolis
	Childs, Donald S., Jr.	Rochester
	Chisholm, Tague C.	Minneapolis
	Chow, Shelley N.	Minneapolis
	Christensen, Clarence H.	Duluth
	Christensen, Eli E.	Winona
	Christensen, Llewellyn E.	Minneapolis
	Christensen, Norman A.	Rochester
	Christenson, Carl E.	Clinton
	Christenson, Leland R.	Maple Plain
	Christian, William L.	Austin
	Christiansen, Harold A.	Jackson
†	Chrzan, Donald J.	Colorado Springs, Colorado
	Chunn, Stanley S.	Willmar
	Church, Gerald E.	Two Harbors
	Cicciarelli, Frances E.	Peoria, Illinois
	Cich, John A.	St. Paul
	Ciriacy, Edward W.	Ely
	Clagett, O. Theron	Rochester
	Clapp, Hubert D.	Crookston
†	Clark, Edward C.	Rochester
	Clark, Elizabeth A. (Mrs. Halbert)	Duluth
†	Clark, Harry B.	St. Cloud
	Clark, Henry B., Jr.	Minneapolis
	Clark, Ivan T.	Duluth
†	Clark, Leslie W.	Manchester, Iowa
	Clark, Malcolm D.	Minneapolis
	Clark, Robert S.	Minneapolis
	Clarke, Dean T.	Faribault
	Clarke, John W.	Waconia
	Clay, Lyman B.	Minneapolis
	Cleaves, William D.	Sauk Centre
	Clifford, George W.	Alexandria
†	Clifton, Theodore A.	Hollywood, Florida
	Closuit, Frederick C.	Aitkin
†	Coburn, William M., Jr.	Phoenix, Ariz.
	Cochrane, Byron B.	St. Paul
	Cochrane, Ray F.	Minneapolis
	Coddon, Walter D.	St. Paul
†	Coder, Donald M.	Rochester
	Cody, D. Thane	Rochester
	Coe, John I.	Minneapolis
	Cohen, Bernard A.	Minneapolis
	Cohen, David F.	London, England
	Cohen, Ephraim B.	Minneapolis
	Cohen, Henry W.	Wayzata
	Cohen, Sumner S.	Minneapolis
	Colby, Malcolm Y., Jr.	Rochester
	Colby, Woodard L.	St. Paul
	Cole, George A.	Albert Lea
	Cole, James S.	Minneapolis
	Cole, Wallace H.	St. Paul
	Coleman, John B.	St. Paul
	Coles, Douglas T.	Rochester
	Coll, James J.	Duluth
†	Colligan, Paul C.	Rochester
†	Collins, Arthur N.	Duluth
	Collins, Roger T.	Roseau
	Colman, Edward L.	Fergus Falls
	Colton, Roger S..	Rochester
†	Comer, Thomas P.	Rochester
	Comfort, Thomas H.	St. Paul
	Conley, Francis W.	Duluth
	Conley, Robert H.	Mankato
	Conlin, F. Dixon	Minneapolis
	Conlon, Daniel C.	Minneapolis
	Connolly, Coleman J.	St. Paul
	Connolly, Daniel C.	Rochester
	Connolly. Joseph P.	South St. Paul
†	Connor, Charles E.	St. Paul
†	Cook, C. Kenneth	St. Paul
	Cook, Edward N.	Rochester
	Coombs, Carl H.	Cass Lake
	Cooper, Charles C.	Moose Lake
	Cooper, John P.	Minneapolis

	Cooper, Robert R.	Minneapolis
	Cooper, Talbert	Rochester
	Cope, Hershel B.	Virginia
	Corbin, Kendall B.	Rochester
†	Corcoran, James R.	Rochester
†	Corniea, Albert D.	Minneapolis
	Correa, Dale H.	Minneapolis
	Corrigan, Cyril J.	Rochester
	Cosgriff, James A.	Olivia
	Cosgriff, James A., Jr.	Olivia
	Cotton, Gerald E.	Fosston
†	Cottor, Robert E.	St. Paul
	Coulter, Harold E.	Minneapolis
†	Countryman, Roger S.	Saratoga, California
	Courteau, Robert D.	Onamia
	Coventry, Markham B.	Rochester
	Coventry, William D.	Duluth
	Covey, Kenneth W.	Crookston
	Cowan, Donald W.	Minneapolis
	Cowan, George M.	Duluth
	Cox, Russell L.	Estherville, Iowa
	Coy, Douglas J.	Grand Rapids
†	Craig, C. C.	International Falls
	Craig, David M.	St. Paul
	Craig, M. Elizabeth	Minneapolis
#	Crandall, Earle E.	San Diego, Calif.
†	Cranmer, Richard R.	Minneapolis
	Cranston, Robert W.	Minneapolis

	Creevy, Charles D.	Minneapolis
	Creps, James R.	Duluth
	Cronwell, Bernhard J.	Austin
	Crow, Earl R.	Minnetonka
	Crow, George M.	International Falls
†	Crowder, Bennett L., II	Rochester
	Crowley, James H.	St. Paul
	Crowley, Leonard V.	Minneapolis
	Crudo, Vincent D.	St. Paul
	Crum, Arthur Z.	St. Paul
	Crump, James W.	St. Paul
	Crusinberry, Charles S.	Des Moines, Iowa
	Cullado, Andrionico F.	Minneapolis
	Cullen, Robert M.	Elmore
	Culligan, John A.	St. Paul
	Culligan, Leo C.	Minneapolis
	Culp, Clyde E.	Rochester
	Culp, Ormond S.	Rochester
	Culver, Lucian G.	St. Paul
	Cumming, E. Dale	St. Paul
	Cumming, Robert J.	St. Cloud
†	Cummins, Ben M.	Rochester
	Cundy, Donald T.	Minneapolis
	Cupps, Roger E.	Rochester
	Curtis, Rauen A.	Le Center
†	Cushing, Richard T.	Ann Arbor, Mich.
†	Cutts, George	Minneapolis
†	Cyrowski, Gerald A.	Rochester

D

	Daehlin, Rolf	Fergus Falls
	Dagg, Earl	Thief River Falls
	Daggett, Donald R.	Minneapolis
†	Dahl, Elmer O.	Minneapolis
	Dahl, James C.	Minneapolis
†	Dahl, John A.	Minneapolis
	Dahlin, David C.	Rochester
	Dale, Allan J. D.	Rochester
	Dale, Les N.	Hastings
†	Dally, Alfred D.	Rochester
†	Daly, Alfred E.	Montgomery
†	Daniel, Donald H.	Minneapolis
	Danielson, Lennox	Litchfield
	Danyluk, Michael	Minneapolis
	Dargay, Cyril P.	Minneapolis
	Daugherty, Guy W.	Rochester
	David, Reuben	Hopkins
†	Davidson, Allan D.	Rochester
	Davidson, Duane J.	Thief River Falls
†	Davidson, Horace B., Jr.	Rochester
†	Davidson, William D.	Minneapolis
†	Davignon, Jean	New York, New York
†	Davis, Austin C.	Pompano Beach, Fla.
	Davis, Edward V.	St. Paul
	Davis, Eunice A.	Bismarck, N. D.
	Davis, George D.	Rochester
†	Davis, Jay C.	Deerfield Beach, Fla.
	Davis, Lloyd T.	Wadena
	Davis, Luther F.	Wadena
	Davis, Michael W.	Minneapolis
	Davis, Raymond D.	Naples, Florida
	Davis, William I.	Moose Lake
	Dawson, James R.	St. Paul
	Dawson, Lorin D.	Worthington
	Dawson, Walter J., Jr.	Minneapolis
	Dearing, William H.	Rochester
	Deason, Keith B.	Chisago City
	Decker, Charles H.	St. Paul

	Decker, David G.	Rochester
	Dedeker, Kenneth L.	Wayzata
†	Dega, Francis J.	Rochester
	Degallier, Daniel	Winona
	Dehnel, Luther L.	St. Cloud
	Delahunty, John R.	Red Wing
	Delano, James G.	Rochester
	Delmore, John L.	Roseau
*	del Plaine, Carlos W.	Minneapolis
	De Marais, Lloyd C.	Hibbing
	Demo, Robert A.	Albert Lea
	De Mordaunt, Paul R.	Rochester
†	Derauf, Benjamin I.	St. Paul
	Derauf, Donald E.	St. Paul
	Derechin, William	St. Paul
†	De Remee, Richard A.	Rochester
	Desai, B. J.	Worthington
†	DeSanto, Lawrence W.	Rochester
	Deters, Donald C.	St. Paul
	Deutsch, Robert J.	Duluth
	Devereaux, Thomas J.	Wayzata
	Devine, Kenneth D.	Rochester
	Devloo, Robert A.	Rochester
	deWerd, Robert W.	Owatonna
	De Weerd, James H.	Rochester
	Deweese, Wilford J.	Bemidji
	Dewey, Donald H.	Owatonna
	Dickman, Roy W.	Minneapolis
	Dickson, Edgar R.	Rochester
	Dickson, Franklin H.	Proctor
	Didier, Edward P.	Rochester
	Diefenbach, Eugene J.	Minneapolis
	Diehl, Harold S.	New York, New York
	Dierker, Heinrich A.	Minneapolis
	Diessner, Ardell W.	Redwood Falls
	Diessner, Grant R.	Rochester
†	Diessner, Henry D.	Minneapolis
	Dietrich, Donald E.	Duluth

#	Dietrich, Robert A.	Augusta, Ga.
	Dille, Donald E.	Litchfield
†	Dillenburg, Cyril J.	Grand Forks, N. D.
	Dillman, Carl E., Jr.	Rochester
	Dinapoli, Robert P.	Rochester
	Dines, David E.	Rochester
	Dinsdale, Howard A.	St. Paul
	Dittrich, Raymond J.	Cambridge
	Divertie, Matthew B.	Rochester
†	Dixon, Claude F.	Rochester
	Doan, Robert E.	Wayzata
	Dobbs, Richard L.	Duluth
	Dobler, Manfred G.	Ely
	Dobson, Mervin W.	Mankato
	Docherty, John A.	Anoka
	Dockerty, Malcolm B.	Rochester
	Docksey, John W	Willmar
	Dodds, William C.	Detroit Lakes
	Dodson, Albertus F.	Brainerd
	Doebler, Myron, I.	Mora
	Doherty, Elmer M.	New Prague
	Dokken, James H.	Windom
	Doman, Victor W.	Lakefield
	Doms, Vernon A.	Elbow Lake
†	Donadio, James V., Jr.	Rochester
	Donaldson, Charles S.	St. Cloud
	Donatelle, Edward P.	Minneapolis
	Donoghue, Francis E.	Rochester
	Donovan, Daniel L.	Albert Lea
†	Dorge, Richard I.	Minneapolis
	Dornbach, Robert A.	Minneapolis
	Dorsey, George C., Jr.	Minneapolis
	Dorsey, William E.	Minneapolis
	Doscherholmen, Alfred	Minneapolis
	Douglas, William W.	Rochester
	Douglass, Bruce E.	Rochester
	Douglass, Jesse E.	Cannon Falls
	Dower, John C.	Rochester
	Downing, Wendell K.	Minneapolis

†	Doxey, Gilbert L.	Minneapolis
	Doyle, James R.	Rochester
*	Doyle, Lawrence O.	Minneapolis
	Drake, Carl B.	St. Paul
	Dredge, Thomas E.	Minneapolis
	Dredge, Thomas E., Jr.	Minneapolis
†	Drexler, Charles J.	Rochester
	Drexler, George W.	Blue Earth
	Drill, Frederick E.	Minneapolis
	Drill, Herman E.	Hopkins
†	Drips, Della G.	Rochester
	Druffner, Charles R.	Rochester
	Dubnow, Morton H.	Rochester
	DuBois, Julian F.	Sauk Centre
	Duff, Edwin R.	Minneapolis
	Dummer, Donald J.	New Brighton
	Duncan, Donald A.	Minneapolis
	Duncan, James W.	Moorhead
	Dunlap, Earl H.	Minneapolis
	Dunn, Robert C.	St. Paul
	Dunstan, Paul L.	Willmar
	Dupont, Joseph A.	Excelsior
	Durkin, John L.	St. Paul
	Duryea, Marbry	Minneapolis
	Duryea, Willis M.	Minneapolis
	Duryea, Willis M., Jr.	Minneapolis
	DuShane, James W.	Rochester
†	Duthoy, E. J.	Bloomington
#	Duval, David L.	Patuxent River, Md.
	Duvall, Arndt J., III	Minneapolis
	Duvoisin, George E.	Rochester
	Dvorak, Benjamin A.	Minneapolis
	Dwan, Paul F.	Minneapolis
	Dworsky, Samuel D.	Minneapolis
	Dwyer, John J.	Duluth
	Dyck, Peter J.	Rochester
	Dyer, John Allen	Rochester
	Dyrdal, Paul J.	St. Paul
	Dysterheft, Adolf F.	Gaylord

E

	Earl, George A.	St. Paul
	Earl, John R.	St. Paul
	Eberley, Tobe S.	Benson
*†	Eberlin, Edward A.	Glenwood
	Eckdale, John E.	Marshall
	Eckman, Philip F.	Duluth
†	Eckman, Philip L.	Rochester
	Eckman, Ralph J.	Duluth
	Eddy, Richard L.	Alexandria
	Eder, Walter P.	Minneapolis
	Edmondson, Hugh A., Jr.	Minneapolis
	Edwards, J. Willard	St. Paul
	Edwards, Jesse E.	St. Paul
	Edwards, Lloyd G.	St. Paul
	Edwards, Thomas J.	St. Paul
†	Edwards, Walter G., Jr.	Rochester
	Eelkema, Herman H.	St. Paul
	Efteland, Myles E.	Minneapolis
	Egge, Sanford G.	Albert Lea
	Eginton, Charles T.	St. Paul
†	Ehrenberg, Claude J.	Minneapolis
	Ehrlich, S. Paul	Minneapolis
	Eich, Matthew A.	Minneapolis
	Eichel, Berkley S.	Shreveport, Louisiana
	Eichenlaub, John E.	Minneapolis
	Eichhorn, Edmund P., Jr.	Minneapolis
†	Eichler, George R.	Rochester

	Eide, O. A.	Hancock
	Eiden, Vera M.	Stillwater
	Eisenman, Walter	Hibbing
	Eisenstadt, David H.	Minneapolis
	Eisenstadt, William S.	Minneapolis
	Eitel, George D.	Minneapolis
†	Ekblad, John W.	Rock Island, Ill.
†	Ekdale, Robert A.	Palo Alto, California
	Eklund, Carl D.	Duluth
	Ekstrand, LeRoy M.	Wabasha
	Eli, Earl W.	Minneapolis
	Elias, Frank J.	Duluth
	Elkins, Earl C.	Rochester
	Ellertson, Leonard M.	Albert Lea
	Ellinger, Albert J.	Willmar
	Ellingson, Richard B.	Minneapolis
	Ellis, Earl W.	Elgin
	Ellis, F. Henry, Jr.	Rochester
*†	Ellison, David E.	Minneapolis
	Ellison, Evan S.	Minneapolis
†	Ellison, Frank E.	Monticello
	Ellwood, Paul M., Jr.	Minneapolis
	Emanuel, Karl W.	Duluth
	Emerson, Edward C.	St. Paul
	Emerson, Edwin E.	Osakis
	Emmett, John L.	Rochester
†	Emmons, Helen J.	Rochester

	Emmons, Robert W.	St. Paul
	Emond, Albert J.	Farmington
	Emond, Joseph S.	Farmington
	Emslander, Richard F.	Rochester
	Endress, Edward K.	St. Paul
	Engberg, Edward J.	Faribault
	Engel, Andrew G.	Rochester
	Engel, Joseph P.	Minneapolis
	Engelhart, Peter C.	Minneapolis
	Engels, Edward P.	Rochester
†	Engelstad, Wendell P.	Duluth
	England, Rodney W.	St. Paul
	Englund, Elvin F.	Minneapolis
	Engstrand, Oscar J.	Minneapolis
	Engstrom, E. Duane	Minneapolis
	Engstrom, George F.	St. Peter
	Engstrom, Robert B.	Mankato
†	Engwall, Richard L.	Minneapolis
	Engroth, Oscar E.	St. Paul
	Eppard, Raymond M.	Cloquet
	Erdal, Ove A.	Albert Lea
	Erich, John B.	Rochester
	Erickson, Alvin O.	Long Prairie
	Erickson, Clifford O.	Minneapolis
	Erickson, Donald J.	Rochester
	Erickson, Laurence F.	Minneapolis
	Erickson, Myron E.	Minneapolis
	Erickson, Reuben F.	Minneapolis
	Erickson, Robert L.	Rosemount
	Erickson, Vernon D.	Grand Rapids
†	Ericson, Swan	Los Angeles, California
	Erlanson, A. Cornell	St. Paul
	Ersfeld, Murray P.	St. Paul
	Esensten, Sidney	Minneapolis
	Espinosa, Raul E.	Rochester
	Estrem, Ralph L.	Fergus Falls
	Estrem, Robert D.	Fergus Falls
	Ettinger, Milton G.	Minneapolis
	Etzwiler, Donnell D.	Minneapolis
†	Eusterman, George B.	Rochester
†	Eusterman, James N.	San Francisco, California
	Eustermann, John J.	Mankato
	Evans, Edward T.	Minneapolis
	Evans, Leslie M.	Sauk Rapids
†	Evans, William B.	Rochester
†	Evarts, Arrah B.	Rochester
	Evensta, John B.	Grand Rapids
	Evison, Emerson O.	Duluth
	Ewens, George B.	Virginia

F

	Faber, John E.	Rochester
†	Fabi, Robert A.	Rochester
†	Fahr, George E.	Minneapolis
	Fairbairn, John F.	Rochester
	Falk, Abraham	St. Paul
†	Fallon, Virgil T.	Minneapolis
	Falls, John L.	Red Wing
	Farber, Lawrence A.	Minneapolis
	Farkas, John V.	St. Paul
	Farley. Harrison H.	Minneapolis
#	Farrell, Francis J., Jr.	Indianapolis, Indiana
†	Farrow, George M.	Rochester
	Fasbender, Herman T.	Hastings
	Faulconer, Albert, Jr.	Rochester
	Fawcett, Arthur M.	Renville
	Fawcett, Keith R.	Duluth
†	Fawcett, Kenneth J.	Rochester
†	Fedor, Robert D.	South St. Paul
	Fee, John G.	St. Paul
	Feeney, John M.	Minneapolis
	Feigal, David W.	Wayzata
	Feigal, William M.	Fairmont
†	Feinberg, Jack H.	Rochester
	Feinberg, Philip	Minneapolis
	Feinberg, Samuel B.	Minneapolis
	Feinstein, Julius Y.	Minneapolis
	Felder, Davitt A.	St. Paul
	Feldmann, Floyd M.	New York, New York
†	Feldt, Robert H.	Rochester
	Felion, Arthur J.	St. Paul
	Fellows, Manley F.	Duluth
†	Felsoory, Attila	Rochester
	Fenger, Ejvind P. K.	St. Paul
	Fenske, Arnold W.	Winona
	Ferguson. John N.	St. Paul
	Ferguson, Richard H.	Rochester
	Ferguson, William C.	Walnut Grove
†	Fernandez, Rafael F.	Rochester
	Ferrell, Clarence R.	Grand Rapids
	Ferris, Deward O.	Rochester
	Fesenmaier, Otto B.	New Ulm
	Fesler, Harold H.	St. Paul
	Fetzek, Albert D.	Minneapolis
	Feuling, John C.	Duluth
	Fiedler, Richard J.	Rochester
	Field, Anthony H.	Savage
	Field, Charles A.	Rochester
	Field, Charles W.	Minneapolis
	Fifer, Ellen Z.	Minneapolis
	Fifer, William R.	Minneapolis
	Fifield. Malcolm M.	Duluth
†	Figi, Frederick A.	Rochester
	Filiatrault, L. J.	Coon Rapids
	Filipovich, Orest N.	Minneapolis
	Finch, J. E.	Mankato
	Fingerman, David L.	Minneapolis
	Fink, Daniel L.	St. Paul
	Fink, Leo W.	Minneapolis
	Fink, Robert J.	Minneapolis
	Fink, Walter H.	Minneapolis
	Finkelnburg, William O.	Winona
†	Finkelstein, Joel	Rochester
	Finley, Paul R.	Minneapolis
#	Finley, Thomas V.	Glasgow, Montana
	Fisch, Herbert M.	Austin
	Fischer, John R.	Blooming Prairie
	Fischer, Mario M.	Duluth
†	Fischer, Robert F.	St. Paul
	Fisher, Dan W.	St. Paul
	Fisher, Don H.	Minneapolis
	Fisher, Isadore I.	Minneapolis
†	Fishman, Norton L.	Rochester
	Fisketti, Henry	Duluth
	Fitch, Charles G.	Worthington
	Fitzsimons, William E.	Brainerd
†	Fjeldstad, C. Alford	Minneapolis
†	Flancher, Leon H.	Crookston
	Flannery, Hubert F.	St. Paul
	Flatt, John R.	Wabasha
	Fleming, Dean S.	Minneapolis
	Flentje, Dale E.	Mankato
	Fletcher, Robert H.	Chisholm

	Fliehr, Richard R.	Minneapolis
	Flinn, James B.	Redwood Falls
*†	Flinn, Thomas E.	Redwood Falls
	Floersch, Adrian J.	Owatonna
	Flom, Reynold P.	St. Paul
	Flom, Robert S.	St. Paul
	Flora, George C.	Minneapolis
	Florence, David W.	Robbinsdale
	Florine, Martin C.	Mankato
	Fluegel, John O.	Rochester
	Flynn, Bernard F.	Hibbing
	Flynn, Louis L., Jr.	St. Paul
	Flynn, Robert A.	St. Paul
	Foderick, Peter P.	Hallock
*†	Fogerty, Charles W.	St. Paul
†	Fogarty, Charles W., Jr.	St. Paul
	Fogelberg, Emil J.	St. Paul
	Foker, Leslie W.	Minneapolis
†	Foley, Frederic E. B.	St. Paul
†	Foley, Ralph B.	Rochester
	Foley, Robert R.	Minneapolis
	Folsom, Louis B.	Minneapolis
	Fontana, Robert S.	Rochester
	Forbes, Edward F.	Minneapolis
	Ford, Burton C.	Marshall
	Ford, W. Harold	Minneapolis
	Forsythe, James R.	St. Paul
†	Forth, Ronald J.	Rochester
	Fortier, George M. A.	Little Falls
	Fortier, Rene G.	Mankato
	Foss, Edward L.	Rochester
	Foster, Orley W.	Minneapolis
	Foulk, William T., Jr.	Rochester
†	Fowler, L. Haynes	Newport Beach, California
	Fox, James Rogers	Minneapolis
	Fox, LeRoy J.	St. Paul
†	Franchere, Frederick W.	Lake Crystal
	Francis, David W.	Morristown
#	Francis, Robert L.	Fullerton, Calif.
	Frane, Donald B.	Minneapolis
	Franklin, Gordon W.	Northome
	Fredericks, George M.	Minneapolis
†	Frederickson, Alice C.	Willmar
	Freeman, Charles D., Jr.	St. Paul
	Freeman, Craig W.	Minneapolis
	Freeman, Donald H.	Mankato
	Freeman, Donald W.	St. Louis Park
†	Freeman, F. Julian	Rochester
†	Freeman, John P.	Glenville
	French, Bayard T.	Hibbing
	French, Lyle A.	Minneapolis
	Frethem, Allen A.	Rochester
	Frey, Richard J.	Minneapolis
	Friberg, Joseph B.	Minneapolis
†	Fricke, Robert E.	Rochester
	Fried, Louis A.	Minneapolis
†	Friedell, Aaron	Minneapolis
	Friedell, George	Minneapolis
	Friedlieb, Oskar P.	Virginia
	Friedman, Harry S.	Minneapolis
#	Friedman, Laurence L.	A.P.O. San Francisco, Cal.
	Friend, Charles A.	Minneapolis
†	Fritsche, Albert	New Ulm
	Fritsche, Carl J.	New Ulm
	Fritsche, Theodore R.	New Ulm
	Fritz, Wallace L.	St. Paul
	Froats, Charles W.	St. Paul
	Frost, John B.	Minneapolis
	Frost, Russell H.	Minneapolis
	Fruchtman, Stanley A.	Minneapolis
	Frye, Charles W.	St. Paul
	Frykman, Howard M.	Minneapolis
	Frys, Russell N.	Minneapolis
	Fulks, Raymond W.	Minneapolis
†	Fuller, Alen M.	Rochester
†	Fuller, Alice H.	Minneapolis
	Fuller, Benjamin F.	St. Paul
	Fuller, Henry, Jr.	Rochester
	Fuller, Josiah	Duluth
	Funk, Victor K.	Hopkins
	Funke, Joyce L.	St. Paul
†	Furlow, William L.	Rochester
	Furman, Christine	Minneapolis
	Furr, Leo	Bird Island
	Fusaro, Ramon M.	Minneapolis

G

	Gaard, Richard C.	Minneapolis
	Gaebe, Milton B.	Clara City
	Gaertner, Frank M. J., Jr.	St. Paul
	Gaida, Joseph B.	St. Cloud
	Gailitis, Veronika M.	St. Paul
†	Gaines, Richard K.	Rochester
	Galbraith, Richard F.	Minneapolis
	Galejs, Aina	Minneapolis
	Gallett, Lester E.	Minneapolis
	Galligan, John J.	St. Paul
†	Galligan, Margaret Mary D.	Minneapolis
	Galloway, Jackson R.	Rochester
	Galway, Charles F.	St. Paul
†	Gambill, Carl M.	Rochester
	Gambill, Earl E.	Rochester
†	Gambill, Harold D.	Rochester
	Gamble, Elbert J.	Albert Lea
	Gamm, Edgar R.	Park Rapids
	Gammell, John H.	Minneapolis
	Garamella, Joseph J.	Minneapolis
	Garber, George L.	Winona
†	Garber, James J.	Rochester
*†	Garbrecht, Arthur W.	St. Paul
	Gardner, Jack K.	Fairmont
†	Gardner, Victor H.	Fairmont
	Gardner, Walter P.	St. Paul
	Garetz, Floyd K.	Minneapolis
†	Garrick, James G.	Rochester
	Garrow, Douglas M.	St. Paul
	Garske, George L.	Minneapolis
	Garten, Joseph L.	Minneapolis
	Garvey, James T.	Minneapolis
†	Gasior, Robert M.	Rochester
	Gasman, David H.	Rochester
#	Gasser, Richard C.	Wichita Falls, Texas
	Gastineau, Clifford F.	Rochester
	Gault, Neal L., Jr.	Minneapolis
†	Gault, Sarah J.	Minneapolis
	Gaute, Svend T.	St. Paul
	Gaviser, David	Minneapolis
	Gedge, Stafford W.	Rochester
	Gehlen, Joseph N.	St. Paul
	Geib, Marvin J.	Fargo, North Dakota
	Geiser, Peter M.	Alexandria

	Geist, Robert W.	St. Paul
#	Gelety, Joseph E.	Lackland AFB, Texas
	Geller, Joseph	Minneapolis
	George, Vane P., Jr.	LeSueur
	Geraci, Joseph E.	Rochester
	Gerend, Thomas J.	Virginia
	Gerstenkorn, George B.	Milaca
	Geurkink, Nathan A.	Rochester
	Geurs, Benjamin R.	Mankato
†	Ghostley, Mary C.	Minneapolis
	Gibbs, Edward C.	St. Paul
	Gibbs, Robert W.	Minneapolis
	Giebenhain, John N.	Minneapolis
	Giere, Joseph C.	Minneapolis
	Giere, Richard W.	Minneapolis
†	Giere, Silas W.	Crookston
†	Giffin, Herbert Z.	Rochester
	Gifford, R. W., Jr.	Cleveland, Ohio
†	Gilbaugh, James H., Jr.	Rochester
	Gilbert, Maurice G.	Minneapolis
	Gilbertsen, A. Sigrid	Minneapolis
	Gilbertsen, Victor A.	Minneapolis
	Gilchrist, Milton R.	St. Paul
†	Gilchrist, Ronald W., Jr.	Rochester
	Gill, Theodore M.	Albert Lea
	Gillespie, Delmar R.	St. Paul
	Gillespie, Malcolm G.	Duluth
	Gillis, Samuel P.	Rochester
	Gilman, Lloyd C.	Willmar
	Gilsdorf, Donald A.	St. Paul
	Gingold, Benjamin A.	Minneapolis
†	Giroux, Jean-Mario	Montreal, Canada
	Gislason, Paul H.	Mankato
	Gislason, Solveig T.	St. Peter
†	Gisvold, John J.	Rochester
	Gjerde, William P.	Lake City
	Glaeser, John H.	Minneapolis
	Glazer, Ira M.	Rochester
	Gleason, Wallace A.	St. Paul
	Glenny, William R.	St. Paul
	Glick, Dallas D.	Mountain Lake
	Glomstad, Gary B.	Deer River
†	Gobel, Fredarick L.	Minneapolis
	Goblirsch, Andrew P.	Sleepy Eye
	Godfrey, H. Wilson	Minneapolis
	Goehrs, Gilman H.	St. Cloud
#	Goethals, Paul L.	Winter Park, Fla.
	Gokcan, Muharrem	Minneapolis
	Gold, David	Minneapolis
	Goldberg, Isadore M.	Minneapolis
	Goldberg, Marvin E.	Minneapolis
	Goldberg, Stanley M.	Minneapolis
	Goldfarb, Benjie L.	Minneapolis
	Goldish, Daniel R.	Duluth
	Goldish, Robert J.	Duluth
	Goldman, Leonard W.	Minneapolis
	Goldman, Theodore I.	Minneapolis
	Goldner, Meyer Z.	Minneapolis
	Goldschmidt, Volker	Duluth
	Goldsmith, Joseph W.	St. Paul
	Goldstein, Alan L.	Hopkins
	Goldstein, Norman P.	Rochester
	Goldston, Edgar C.	Rochester
*†	Goltz, Edward V.	St. Paul
	Goltz, Robert W.	Minneapolis
	Good, C. Allen, Jr.	Rochester
	Good, Gary	Minneapolis
	Good, Roy H.	Northfield
	Goodchild, William R.	Minneapolis
*†	Goodman, Charles E.	Virginia
	Goodman, Ernest	St. Paul
	Goodnow, William H.	Duluth
	Gordon, John R.	Minneapolis
†	Gordon, Michael S.	Rochester
	Gordon, Philip E.	Minneapolis
†	Gordon, Richard S.	Rochester
	Gordon, Sewell S.	St. Louis Park
	Gould, Allan B., Jr.	Rochester
	Govrik, Kalman	St. Paul
	Gowan, Lawrence R.	Duluth
†	Gowan, Lawrence R., Jr.	Rochester
	Gracey, Douglas R.	Rochester
†	Graham, Archibald W.	Chisholm
	Graham, Asa B.	Faribault
	Grahek, Jack P.	Ely
	Granquist, Richard D.	Minneapolis
	Grant, John C.	Sauk Centre
	Grant, Suzanne	Minneapolis
†	Gratzek, Frank R.	Anoka
†	Graves, Richard B.	Red Wing
†	Gray, Edward F.	Wawautosa, Wis.
	Gray, Royal C.	Minneapolis
	Green, Clayton R.	Excelsior
†	Green, George R.	Rochester
	Green, Paul A.	Rochester
	Green, Robert A.	St. Louis Park
	Greenberg, Albert J.	Minneapolis
†	Greenberg, Eugene	Rochester
	Greene, Daniel E.	Warren
	Greene, Gordon	Arlington
†	Greene, Jerry G.	Rochester
	Greene, Laurence F.	Rochester
	Greene, Leonard H.	Minneapolis
	Greenfield, Irving	Minneapolis
	Greenfield, William T.	Cokato
†	Greenough, William G.	St. Paul
	Gregg, James A.	Rochester
	Gregoire, Earl	Bemidji
†	Greisheimer, Esther M.	Philadelphia, Pa.
	Gretsch, Gerald A.	St. Paul
	Gridley, John W.	St. Peter
	Griebie, Grant L.	Brownton
	Griffin, John W.	Bemidji
	Griffin, Richard P.	Benson
	Griffin, Thomas M.	St. Paul
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	Grimes, Burton P.	St. Peter
	Grimes, Marian	Minneapolis
	Grimes, Paul T.	Park Rapids
	Grimmell, Francis J.	Minneapolis
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	Grinley, Andrew V.	Grand Rapids
	Grinvalds, Anna O.	Cambridge
	Grismer, Jerome T.	Minneapolis
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	Gronquist, Y. K. J.	Cloquet
	Gronvall, Paul R.	Hopkins
	Groschupf, Richard P.	Bemidji
†	Groschupf, Theophilus P.	Bemidji
	Grose, Frederick N.	Clarissa
	Gross, John B.	Rochester
	Grotting, John K.	Minneapolis
	Gruys, Robert I.	Wells
	Guenther, Dean E.	West St. Paul
	Guilfoile, Pierre J.	Delano
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	Gunlaugson, Frederick G.	Minneapolis

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	Gustafson, Robert W.	Granite Falls
	Gustason, Harold T.	Minneapolis
	Gustilo, Ramon B.	Minneapolis
	Guthrie, J. Cameron	St. Paul
	Guy, Jack A.	New London

H

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	Hable, Orville A.	Buffalo Lake
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	Haesly, Warren W.	Winona
	Hagberg, Norman L.	Montevideo
	Hagedorn, Albert B.	Rochester
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	Hagen, Kristofer	Minneapolis
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	Hagen, Wayne S.	Minneapolis
	Haglin, John J.	Minneapolis
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†	Haines, Samuel F.	Rochester
	Hakanson, Erick Y.	St. Paul
	Halbert, John J.	Duluth
	Halenbeck, Philip L.	St. Cloud
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	Hall, George M.	Bemidji
	Hall, Harry B.	Minneapolis
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	Hall, Wendell H.	Minneapolis
	Hallberg, Olav Erick	Rochester
	Hallenbeck, George A.	Rochester
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	Hallin, Roger P.	Minneapolis
†	Halloran, Walter H.	Jackson
	Halme, William B.	Wadena
	Halper, Bernard	Hibbing
	Halpern, David J.	Brewster
	Halpin, Joseph E.	Rush City
	Halverson, Donald E.	Winnebago
	Halverson, Kermit J.	Parkville
	Halverson, William G.	Madelia
	Halvorsen, Daniel K.	Owatonna
	Halvorson, David C.	Northfield
	Halvorson, James W.	Zumbrota
	Hambridge, Gove, Jr.	Minneapolis
	Hamel, Arnold L.	Minneapolis
	Hamel, Joseph I.	Minneapolis
	Hammar, Lawrence M.	Mankato
	Hammarsten, James F.	St. Paul
	Hammerstrom, Robert N.	Minneapolis
	Hammes, Ernest M.	St. Paul
	Hammes, Ernest M., Jr.	St. Paul
	Handler, Seymour	Minneapolis
	Hankerson, Robert G.	Minnesota Lake
	Hanlon, David G.	Rochester
	Hannah. Hewitt B.	Minneapolis
	Hannon, Donald W.	St. Paul
	Hanover, Ralph D.	International Falls
	Hansen, Cyrus O.	Minneapolis
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	Hansen, Milo L.	Little Falls

†	Hansen, Olga S.	Minneapolis
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	Hansen, Robert E.	Hibbing
	Hansen, Rollin M.	Minneapolis
	Hansen, Theodore M.	Albert Lea
	Hanske, Edward A.	Minneapolis
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	Hanson, Harold B.	Minneapolis
	Hanson, Harold W.	Minneapolis
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	Hanson, John W.	Northfield
	Hanson, Lewis	Frost
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	Hanson, Mark C. L.	Minneapolis
	Hanson, Mildred S.	Minneapolis
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	Hanson, William B.	Minneapolis
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	Hargraves, Malcolm M.	Rochester
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†	Harrington, Stuart W.	Rochester
	Harrington, Vernon A.	Duluth
	Harris, John E.	Minneapolis
	Harris, Leon D.	Minneapolis
	Harris, Lloyd E.	Rochester
	Harrison, Carlos E.	Rochester
	Harrison, Edgar G., Jr.	Rochester
	Harrison, Percy W.	Worthington
	Harrison, William C.	Minneapolis
	Hart, William E.	Monticello
	Hartfiel, William F.	St. Paul
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	Hartig, Marjorie	St. Paul
	Hartig, Paul R.	Minneapolis
	Hartjen, Jason K.	Bemidji
	Hartman, Evelyn E.	Minneapolis
	Hartnagel, Grant F.	Red Wing
	Hartridge, Virginia B.	Rochester
	Hartung, Elmer H.	Claremont
	Hartwich, Roger F.	Winona
	Hartwig, John A.	Minneapolis
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	Hartville, Donald D.	Rochester
	Hass, Frederick M.	Minneapolis
	Hastings, Donald W.	Minneapolis
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	Haugan, Norman R.	Park Rapids
	Hauge, Erling T.	Minneapolis
	Hauge, Malvin I.	Clarkfield
	Haugen, George W.	Minneapolis
	Haugen, John A.	Minneapolis
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†	Hauser, Victor P.	St. Paul
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	Havel, Robert J.	Minneapolis

	Haven, Walter K.	Minneapolis
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†	Havens, John G. W.	Minneapolis
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	Hawkinson, Harlan W.	St. Paul
	Hawkinson, Raymond P.	Minneapolis
	Hawley, George M. B., II	Red Wing
	Hay, Lyle J.	Minneapolis
	Hayes, Albert F.	St. Paul
	Hayles, Alvin B.	Rochester
	Hays, Albert T.	Minneapolis
†	Hays, James C.	Rochester
	Haywa, E. William	Minneapolis
	Head, Douglas P.	Minneapolis
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#	Heaton, John W., Jr.	Oxford, England
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†	Heck, Frank J.	Wakefield, New Hampshire
	Heck, William W.	St. Paul
	Hedemark, Homer H.	Ortonville
	Hedemark, Truman A.	Ortonville
	Hedenstrom, Charles W.	St. Paul
	Hedenstrom, Frank G.	St. Paul
	Hendenstrom, Paul H.	St. Cloud
	Hedenstrom, Philip C.	Marshall
	Hedenstrom, Richard H.	St. Paul
	Hedlund, Charles J.	St. Paul
	Hedrick, William L.	Minneapolis
	Heegaard, William G.	Alexandria
	Hegstad, Thomas C.	Windom
	Heiam, William C.	Cook
	Heiberg, Olaf M.	Worthington
	Heid, James K.	Little Falls
†	Heidel, Werner	Rochester
	Heilig, William R.	St. Paul
	Heimark, John J.	Mankato
	Heinz, Ivy B.	Shakopee
	Heinzerling, Carl R.	Chaska
	Heise, Carl vR.	Winona
	Heise, Herbert vR.	Winona
	Heise, Paul vR.	Winona
	Heise, Philip vR.	Winona
	Heise, William vR.	Winona
	Heller, Edgar E.	Mankato
	Helseth, Hovald K.	Fergus Falls
#	Helseth, Hovald K., Jr.	Minneapolis
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	Hempel, Dean J.	Minneapolis
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	Henderson, John W.	Rochester
	Henderson, Lowell L.	Rochester
	Henderson, Terrance P.	White Bear Lake
	Hendricks, Esten J.	Verndale
	Hengstler, William H.	St. Paul
	Henke, Wilbert J.	St. Paul
	Henrikson, Earl C.	Minneapolis
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	Henry, Harold W.	Hinckley
	Henry, James S.	St. Paul
	Henry, John C.	Owatonna
	Henry, Joseph E.	Milaca
	Henry, Kenneth G.	Owatonna
	Henry, Richard T.	Crosby
	Henwood, Wesley C.	Virginia
	Hepper, Norman G.	Rochester
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	Herbert, Willis L.	Minneapolis
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	Hermann, Harold W.	Minneapolis
*†	Hermanson, Peter E.	Hendricks
	Herrick, Donald W.	St. Paul
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*	Hertz, Myron J.	St. Paul
	Hesla, Inman A.	Austin
	Hess, Carroll N.	Minneapolis
	Hetzler, John A.	St. Paul
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†	Hewitt, Richard M.	Rochester
	Hiatt, John A.	Minneapolis
	Hickok, David F.	Minneapolis
	Higdon, Donald A.	St. Cloud
	Higgins, John A.	Rochester
	Hildebrand, John E.	Bemidji
†	Hildebrand, Lawrence D.	Minneapolis
†	Hildebrandt, Walter C.	Minneapolis
	Hilding, Anderson C.	Duluth
	Hilgedick, William R.	Chisago City
	Hilger, Jerome A.	St. Paul
	Hilger, Laurence D.	St. Paul
	Hilgermann, George O.	Minneapolis
†	Hilgers, Robert D.	Chicago, Ill.
	Hilker, Marcus D.	St. Paul
	Hilker, Robert T.	Owatonna
	Hill, Charlotte W.	St. Paul
	Hill, Earl	Minneapolis
	Hill, Elmer M.	Minneapolis
†	Hill, Frederick E.	Riverside, California
	Hill, John R.	Rochester
	Hill, Richard W.	Rochester
*†	Hillis, Samuel J.	E. Bradenton, Fla.
	Hinckley, Robert G.	Minneapolis
	Hinderaker, Harris P.	Willmar
	Hines, Edgar A., Jr.	Brevard, N. C.
	Hiniker, Louis P.	St. Paul
	Hiniker, Peter J.	Le Sueur
	Hinz, Walter E.	Willmar
†	Hirschboeck, Frank J.	Duluth
	Hirsh, Stanton A.	Crookston
	Hitchcock, Claude R.	Minneapolis
	Ho, Shu Kang	St. Paul
	Hochfilzer, John J.	St. Paul
	Hodapp, Robert V.	Willmar
	Hodges, Kenneth V.	Minneapolis
	Hodgson, Corrin H.	Rochester
	Hodgson, Jane E.	St. Paul
	Hodgson, John R.	Rochester
	Hoeg, Dwight C.	Duluth
	Hoeper, Philip G.	Mankato
	Hoff, Herbert O.	Duluth
	Hoffbauer, Frederick	Minneapolis
	Hoffert, Henry E.	Minneapolis
	Hoffman, David L.	Rochester
	Hoffman, Harry N., II	Rochester
	Hoffman, Roy A.	Minneapolis
	Hoffman, Walter Lees	Minneapolis
	Hofmann, Gerald N.	Minneapolis
	Hogan, Henry W., Jr.	Crookston
	Hoganson, Donald E.	Bemidji
	Hohmann, Albert	St. Paul
†	Hoidale, Andrew D.	Tracy
	Holbrook, Margaret A.	Rochester
†	Holcomb, Joel T.	Marine-on-St. Croix
†	Holcomb, O. William	St. Paul
	Holian, Darwin K.	Albert Lea
	Holland, C. R.	Rochester

	Hollenhorst, Robert W.	Rochester
	Holley, Keith E.	Rochester
	Hollinshead, W. H.	St. Paul
†	Hollowell, O. Weems	Rochester
	Holm, Owen W.	Crookston
	Holman, Colin B.	Rochester
	Holmberg, Conrad J.	Minneapolis
†	Holmberg, LeRoy J.	Canby
	Holmen, Robert W.	St. Paul
*	Holmes, Alva E.	Rush City
	Holmstrom, Carle H.	Warren
	Holt, John E.	St. Paul
	Holten, John	Moorhead
	Holzapfel, Fred C.	Minneapolis
	Hom, Leong Y. W.	Battle Lake
	Honath, Donald H.	Owatonna
	Hoover, Norman W.	Rochester
#	Hopkins, Donald M.	Chelsea, Mass.
	Hopkins, G. Wendell	Minneapolis
	Hopperstad, J. Jerome	Minneapolis
	Hoppes, Emerson E.	Minneapolis
†	Horner, Bennett A.	Rochester
†	Horner, Frances A.	Rochester
	Horns, Howard L.	Minneapolis
	Horns, Richard C.	Minneapolis
†	Horton, Bayard T.	Rochester
	Horton, Robert R.	Santa Barbara, Calif.
	Hoseth, Wayne L.	Minneapolis
	Hottinger, George C.	Minneapolis
	Hottinger, Raymond C.	Janesville
†	Houglum, Arvid J.	St. Paul
†	Houkom, Bjarne	Minneapolis
	Houkom, S. Sverre	Duluth
	Houle, Rollin J.	New Brighton
	Houlton, William H.	St. Paul
†	Houston, Hal E., Jr.	Rochester
	Houts, Joseph C.	Dassel
	Hovde, Gordon W.	Lindstrom
*	Hovde, Rolf	Winthrop
	Hovland, Melvin L.	Minneapolis
	Hovland, Richard D.	Minneapolis
	Howard, Frank M., Jr.	Rochester
	Howard, Marshall I.	Mankato
†	Howard, Merrill A.	St. Paul
	Howard, Robert B.	Minneapolis
	Howard, Solomon E.	Minneapolis
	Howe, Newell W.	West St. Paul
	Howell, Carter W.	Minneapolis
	Howell, Llewelyn P.	Rochester
	Hoyer, Ludolf J.	Windom
	Hoyt, C. Sherman	Minneapolis
	Hruza, William J.	Madelia
	Huber, Robert W.	St. Croix Falls, Wisconsin
	Hubin, Edwin G.	Sandstone
	Hudec, Elwyn R.	Echo
†	Hudgins, Robert L.	Rochester
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	Huebert, Dan W.	Hutchinson
†	Huenekens, Edgar J.	Minneapolis
	Huff, John S.	Minneapolis
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	Huffington, Herb L.	Waterville
	Hughes, Bernard J.	St. Cloud
†	Hughes, Rollin W., Jr.	Rochester
	Hughes, Sidney O.	Winona
	Huizenga, Kenneth A.	Rochester
†	Hulteng, Donald B.	Minneapolis
	Hultkrans, Rudolph E.	Minneapolis
	Hunder, Gene G.	Rochester
	Hunt, Arthur B.	Rochester
	Hunt, James C.	Rochester
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	Hunt, Vincent R.	Red Lake Falls
	Hunter, Murray H.	Farmington
	Hunter, Samuel W.	St. Paul
	Hurr, Maland C.	Minneapolis
	Hurwitz, Milton M.	St. Paul
	Huseby, Thomas L.	St. Paul
	Husebye, Kjeld O.	St. Paul
	Hustad, Edward G.	Minneapolis
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	Hutchinson, Henry	Moose Lake
†	Hutton, Frederick A.	Rochester
	Hymes, Charles	Minneapolis

I

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	Ide, Arthur W., Jr.	Minneapolis
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	Iverslie, Philip C.	Minneapolis
	Iverson, Eleanor B.	Minneapolis
	Iverson, Rolf M.	Minneapolis
	Ivins, John C.	Rochester
	Ivy, Horace K.	Rochester

J

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	Jacklin, Alexander J.	Duluth
	Jackman, Raymond J.	Rochester
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	Jackson, Richard L.	Minneapolis
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	Jacobs, Douglas L.	Willmar
	Jacobson, Clarence	Chisholm
	Jacobson, Clifford W.	Breckenridge
	Jacobson, Ferdinand C.	Duluth
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	James, Ellery M.	St. Paul
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	Janda, George W., Jr.	Minneapolis
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	Janecky, Allen G.	Baudette
†	Janes, Donald R.	Rochester
	Janes, Joseph M.	Rochester
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	Janssen, Martin E.	St. Paul
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	Jarvis, Charles W.	St. Paul
	Jastram, Rupert M.	St. Paul
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	Jefferies, William L.	St. Louis Park

	Jensen, Alvin M.	Brownton
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	Jensen, John A.	Crookston
	Jensen, Nathan K.	Minneapolis
	Jensen, Paul A.	Minneapolis
	Jensen, Reynold A.	Hopkins
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	Jensen, James E.	Stillwater
	Jepson, William W.	Minneapolis
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	Jerome, Elizabeth B. K.	Minneapolis
	Jeronimus, Henry J.	Duluth
	Jessico, Charles M.	Duluth
	Jeub, Robert P.	Minneapolis
	Joffe, Harold H.	Virginia
	Johanson, Waldemar G.	St. Paul
	Johnson, Alan R.	Windom
	Johnson, Aldridge F.	Isle
	Johnson, Angelo G.	Minneapolis
	Johnson, Arthur B.	Minneapolis
	Johnson, Arthur G., Jr.	Fergus Falls
	Johnson, Calvin J.	Grand Rapids
	Johnson, Carl Edwin	St. Paul
	Johnson, Carl Eric	Rochester
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	Johnson, C. Percy	Tyler
	Johnson, Curtis M.	Winona
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	Johnson, Donald A.	Minneapolis
	Johnson, Douglas L.	Little Falls
	Johnson, Edward A.	Minneapolis
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	Johnson, Einer W., Jr.	Rochester
	Johnson, Emil	Stillwater
	Johnson, Frank E.	Minneapolis
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	Johnson, Gordon E.	Minneapolis
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	Johnson, Leonard F.	Winona
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	Johnson, Norton T.	Minneapolis
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	Johnson, Reinald G.	Minneapolis
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	Johnson, Richard J.	St. Paul
	Johnson, Richard S.	Minneapolis
	Johnson, Robert E.	Minneapolis
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	Johnson, Victor	Rochester
	Johnson, Vilhelm M.	Dawson
	Johnson, Walter K.	New Kensington, Pa.
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	Johnson, William J.	Rochester
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†	Jones, H. Royden, Jr.	Rochester
†	Jones, Harry F.	Rochester
†	Jones, Herbert W., Jr.	Minneapolis
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	Jones, Richard H.	Minneapolis
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	Jordan, Donald V.	Minneapolis
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	Jordan, Lewis S.	Granite Falls
	Jorgensen, Harlan	Minneapolis
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	Joseph, Arnold H.	St. Paul
	Joyce, George L.	Rochester
	Joyce, John W.	Rochester
	Judd, Allen S.	Minneapolis
	Judd, Edward S.	Rochester
	Judd, Walter H.	Washington, D. C.
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	Juergens, John L	Rochester
	Juergens, Manley F.	Stillwater
	Juers, Edward H.	Red Wing
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	Juntunen, Roy R.	Duluth
	Jurdy, Mitchell	Minneapolis
	Just, Herman J.	Hastings

K

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†	Kabrick, Ola A.	Hull, Illinois
	Kadesky, Harold B.	Minneapolis
	Kaese, Werner E.	Rochester
†	Kaiser, Harold B.	Los Angeles, California
	Kaiser, Milton L.	New Ulm
	Kalb, Thomas J.	Minneapolis
	Kallestad, Leonard L.	Wayzata
	Kane, Dennis J.	St. Paul
	Kanne, Earl R.	Brainerd
	Kantar, Bruce L.	Minneapolis
	Kaplan, David H.	Minneapolis
	Kaplan, Harold A.	Minneapolis
	Kaplan, J. Jacob	Minneapolis
	Kapsner, Adrian L.	Hutchinson
	Kapsner, Alfred T.	Princeton
	Karges, Laurel E.	Grand Rapids
	Karish, Louis J.	Grand Rapids
	Karleen, Conrad I.	Minneapolis
	Karlen, Markle	Minneapolis
	Karn, Jacob F.	Ortonville
	Karnes, William E.	Rochester
	Karon, Everett H.	St. Paul
	Karon, Irvine M.	St. Paul
	Kasper, Eugene M.	St. Paul
	Kasper, Robert E.	Minneapolis
	Kath, Reinhard H.	Arlington
	Katkov, Harold	Wayzata

	Katz, Louis J.	Long Beach, California
	Kaufman, Edward J.	Appleton
†	Kaufman, Herschel J.	Cincinnati, Ohio
	Kaufman, Walter B.	Mankato
†	Kaufman, William C.	Appleton
	Kavanaugh, Gerald J.	Rochester
	Kazmier, Francis J.	Rochester
	Kearney, R. Wynn	Mankato
	Kearns, Thomas P.	Rochester
	Keating, F. Raymond	Rochester
	Keil, Marcus A.	Albert Lea
	Keith, Haddow M.	Rochester
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	Kelly, Charles F.	Minneapolis
	Kelly, Edward H.	St. Paul
	Kelly, Helen M.	St. Paul
	Kelly, James H.	St. Cloud
	Kelly, John C.	Minneapolis
	Kelly, John F.	Cold Spring
	Kelly, John P.	Minneapolis
	Kelly, John T.	Minneapolis
	Kelly, Joseph R.	St. Paul
	Kelly, Patrick J.	Rochester
	Kelly, Robert T.	Grand Rapids
†	Kelsey, Carleton G.	St. Paul
	Kelsey, Chauncey M.	St. Paul
†	Kemp, Alphonse F.	Mankato
	Kempers, Roger D.	Rochester
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	Kennedy, Byrl J.	Minneapolis
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†	Kennedy, Claude C.	Minneapolis
	Kennedy, George L.	Faribault
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	Kennedy, William R.	Minneapolis
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	Kerr, Frederick W. L.	Rochester
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	Kettering, Ronald F.	Rochester
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	Keyes, Robert W.	Pipestone
	Kiely, Joseph M.	Rochester
	Kierland, Robert R.	Rochester
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	Kimmel, George C.	Minneapolis
	Kincaid, Owings	Rochester
	King, Frances W.	Hopkins
†	King, John N.	Rochester
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	Kinney, Vernard R.	Rochester
	Kinsella, Thomas J.	Minneapolis
	Kiolbasa, Edward B.	Stillwater
	Kippen, Neil	Breckenridge
	Kirby, Thomas J., Jr.	Rochester
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	Klass, Donald W.	Rochester
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	Klein, William A.	Duluth
	Kleinsasser, Warren L.	Farmington
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†	Kline, Richard J.	Rochester
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	Knapp, Miland E.	Minneapolis
	Knapp, Robert D., Jr.	Rochester
†	Knight, Ralph T.	Minneapolis
†	Knight, Ray R.	Minneapolis
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	Knipp, William J.	Brainerd
	Knoche, Harvey A.	Gaylord
	Knoedler, John P.	Duluth
	Knoll, W. V.	Brainerd
	Knudsen, Helen L.	Minneapolis
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	Knudson, Lewis A.	Spring Grove
	Knutson, Robert C.	St. Paul
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	Kodres, Nina	St. Paul
	Koelsche, Giles A.	Rochester
	Koenig, Robert P.	St. Cloud
	Kohlbry, Carl O.	Duluth
	Kohlhase, Robert E.	Minneapolis
	Kolars, Charles P.	Minneapolis
	Kolars, James J.	Faribault
†	Koller, Hermann M.	Minneapolis
†	Koller, Louis R.	Minneapolis
	Koller, Robert L.	Minneapolis
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	Kooda, Jennings C.	Morris
	Koons, William R.	Mahnomen
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	Korchik, John P.	Minneapolis
	Korda, Henry A.	Pelican Rapids
	Kosiak, Michael	St. Paul
	Kosiak, William	Two Harbors
	Kostick, William R.	Fertile
	Kotchevar, Frank R.	Eveleth
	Kottke, Bruce A.	Rochester
	Kottke, Frederic J.	Minneapolis
	Kotval, Russell J.	Pipestone
	Koucky, Rudolph W.	Minneapolis
	Koutsky, Carl D.	Minneapolis
	Kovack, Freeman D.	Minneapolis
	Kozak, Michael J.	Minneapolis
	Koza, Donald W.	St. Paul
	Kozel, William J.	Morris
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	Kraemer, George N.	Fairmont
	Krafft, Walter E.	Minneapolis
	Kragh, Lyle V.	Minneapolis
	Kramer, James D.	St. Paul
	Krause, Carl W.	Fairmont
	Kremen, Arnold J.	Minneapolis
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†	Kucera, William J.	Santa Barbara, California
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	Kuhlmann, Lawrence B.	Melrose
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	Kusske, Douglas R.	St. Paul
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	Kvistberg, Gerald K.	St. Cloud
	Kyle, Robert A.	Rochester

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	Lannin, Donald R.	St. Paul
	Lansky, Shirley A.	St. Paul
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	Larson, Ernest J., Jr.	Minneapolis
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	Larson, Keith D.	Moose Lake
	Larson, Kenneth R.	St. Paul
	Larson, Lawrence M.	Minneapolis
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	Larson, Leonard M.	Minnetonka
	Larson, Leroy J.	Bagley
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	Larson, Wyllis G.	Minneapolis
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	Latts, Elliot M.	Minneapolis
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	Lee, Hubert W.	Brainerd
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	Lenz, Oa	Minneapolis
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	Leonard, Samuel	Minneapolis
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	Lester, Theodore H.	Minneapolis
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	Leverenz, Carleton W.	St. Paul
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	Lewis, Charles W.	Henning
†	Lewis, Donald L.	Rochester
	Lewis, Glenn M., Jr.	St. Paul

	Lewis, Joyce S., Jr.	St. Paul
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	Lien, Richard J.	St. Paul
	Lienke, Roger I.	Robbinsdale
	Liffrig, William W.	Red Wing
†	Lightbourn, Edgar L.	Hastings
	Lilleberg, Norbert J.	St. Paul
	Lillehei, C. Walton	Minneapolis
	Lillehei, Richard C.	Minneapolis
	Lillie, Andrew R.	St. Paul
	Lillie, John C.	Rochester
	Lima, Ludvig R.	Montevideo
	Limbeck, Donald A.	Minneapolis
	Lindahl, Merlyn J.	Sherburn
	Lindberg, Alfred L.	Wheaton
	Lindberg, Vernon L.	Minneapolis
	Lindberg, Winston R.	Minneapolis
	Lindblom, Alton E.	North Mankato
	Lindblom, Maurice L.	Minneapolis
	Lindeland, Arthur T.	Minneapolis
	Lindell, Robert E.	St. Paul
	Lindeman, Raymond J.	Paynesville
	Lindemann, Charles E.	Minneapolis
	Linderholm, Bruce E.	Minneapolis
	Lindgren, Russell C.	Minneapolis
	Lindley, Stanley B.	St. Cloud
	Lindquist, Dale C.	Lindstrom
	Linquist, Max F.	South St. Paul
	Linquist, Richard H.	Minneapolis
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	Lindseth, Esten O.	St. Paul
	Linke, Charles A.	Duluth
	Linke, Clara L.	Duluth
	Linner, Gunnar	Minneapolis
	Linner, John H.	Minneapolis
	Linner, Paul W.	Minneapolis
	Linscheid, Ronald L.	Rochester
	Lippman, Hyman S.	St. Paul
	Lippmann, Elmer W.	Hutchinson
	Lipschultz, Oscar	Minneapolis
	Lipscomb, Paul R.	Rochester
	Litin, Edward M.	Rochester
	Litkewitsch, Helene	St. Paul
	Litman, Abraham B.	Minneapolis
	Litman, Samuel N.	Duluth
	Litman, Thomas	Minneapolis
	Litzow, Thaddeus J.	Rochester
	Lober, Paul H.	Minneapolis
	Loeb, George	St. Cloud
	Loes, Louis A.	St. Cloud
	Lofgren, Eric P.	Rochester
	Lofgren, Karl A.	Rochester
	Lofsness, Stanley V.	Minneapolis
†	Lofstrom, Dennis E.	St. Paul
	Logan, George B.	Rochester
†	Logefeil, Rudolph C.	Minneapolis
	Logothetis, John A.	Minneapolis
	Lohmann, John G.	Pipestone
	Loken, Merle K.	Minneapolis
	Loken, Selmer M.	St. Paul
	Loken, Theodore	Ada
	Lommen, Morris L.	Austin
†	Lommen, Peter A.	Austin
	Lommen, Peter A., Jr.	Austin
†	Long, Richard J.	Rochester
	Longfellow, Helen W.	Brainerd
†	Longo, Margaret F.	Rochester
	Loomis, George L.	Winona
	Lorentzen, Ernest S.	Detroit Lakes
	Lott, Frederick H.	Minneapolis
	Louisell, Charles T.	Fairmont
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	Love, J. Grafton	Rochester
†	Lovett, Beatrice R.	Minnetonka
	Lowe, Alexander D.	South St. Paul
*	Lowe, Earl R.	South St. Paul
†	Lowe, Stanley W.	Rochester
	Lowe, Thomas A.	South St. Paul
	Lowry, Elizabeth C.	Minneapolis
	Lowry, Jeanette K.	Minneapolis
	Lowry, Paul T.	Minneapolis
	Lowry, Thomas	Minneapolis
	Lu, Cheng-en	Fergus Falls
	Luby, Thomas H.	St. Cloud
†	Luck, Hilda	Mankato
	Lueck, Wallace W.	Minneapolis
†	Lufkin, Murray W.	Rochester
	Lufkin, Nathaniel H.	Minneapolis
	Luh, Edwin F.	St. Paul
	Lukk, Olaf	Prior Lake
	Lund, Carl J. T.	Fergus Falls
	Lund, George W.	Minneapolis
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	Lund, Werner J.	Staples
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†	Lundblad, Roy A.	Minneapolis
	Lundblad, Stanley W.	Minneapolis
	Lundborg, Richard O.	Rochester
†	Lundeberg, Karl R.	Minneapolis
	Lundell, Carl L.	Granite Falls
	Lundholm, Arthur M.	Harris
	Lundquist, Curt W.	Owatonna
	Lundquist, Virgil J. P.	Minneapolis
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†	Lynch, Matthew J.	Minneapolis
	Lynch, Michael F.	Minneapolis
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	Lynn, Hugh B.	Rochester
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	Lysne, Myron	Minneapolis
	Lysne, Richard B.	Minneapolis
	Lysyj, Anatol	Minneapolis
	Lyzenga, Anton G.	Minneapolis

M

McBean, James B.	Rochester
McCaffrey, F. John	Minneapolis
McCain, Donovan L.	St. Paul
McCallister, Ben D.	Rochester
McCampbell, Malcolm D.	Minneapolis
McCannell, Malcolm A.	Minneapolis

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	McCarthy, Austin M.	Willmar
	McCarthy, Charles J.	St. Paul
	McCarthy, Donald	Fort Snelling
	McCarthy, Laurence J.	Rochester
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	McGoon, Dwight C.	Rochester
	McGovern, William A., Jr.	St. Cloud
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	McMurtrie, William B.	Minneapolis
	McNamara, John P.	Rice
	McNear, George R., Jr.	Heron Lake
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	McNeill, John A.	St. Paul
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#	McRoberts, Jerry W.	Bremerton, Wash.
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†	MacDonald, Daniel A.	Minneapolis
	MacDonald, Roger A.	Grand Marais
	MacKinnon, Donald C.	Minneapolis
	MacLean, Alexander R.	Rochester
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	Mach, Frank B.	Minneapolis
	Mach, John R.	Minneapolis
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	Mackoff, Samuel	Phoenix, Ariz.
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	Mahle, James P.	Minneapolis
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	Mann, George A.	Minneapolis
	Manning, Preston C., Jr.	Columbia, S. C.
	Manoles, Elias N.	Minneapolis
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	Martin, David E., III	Wabasha
	Martin, Doreen A.	Pepin, Wisconsin
	Martin, Dwight D.	St. Paul
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	Martin, George R.	Minneapolis
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	Martin, John T.	Rochester
	Martin, Maurice J.	Rochester
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	Martinson, Elmer J.	Wayzata
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†	Masson, James C.	Rochester

	Masson, James K.	Rochester
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	Mattison, Percy A.	Winona
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	Meekin, Patrick C.	Minneapolis
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	Meinert, John K.	Willmar
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	Meller, Maurice	Brainerd
	Meller, Robert L.	Minneapolis
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	Mensheha, Nicholas M.	Minneapolis
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	Menold, William F.	St. Paul
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	Mercil, William F.	Crookston
	Meredith, Donald C.	Mankato
†	Meredith, John	Rochester
†	Merkert, Charles E.	Minneapolis
	Merner, Thomas B.	Minneapolis
†	Merrick, Charlotte T.	St. Paul
	Merrick, William G.	Duluth
	Merrill, Robert W.	Morris
	Merritt, Wallace A.	Rochester
	Messenheimer, Myron G.	Minneapolis
	Metcalf, Norman B.	Princeton
	Metz, Donald D.	Minneapolis
	Meyer, Alvin J.	Minneapolis
†	Meyer, E. Lawrence	Winona
	Meyer, Frederick C.	Kenyon
	Meyer, Howard J.	Duluth
	Meyer, Paul F.	Faribault
	Meyer, Richard H.	Faribault
	Meyer, Robert P.	Faribault
†	Meyerding, Henry W.	Rochester
†	Michael, Joseph C.	Minneapolis
	Michel, Henry H.	Minneapolis
	Michels, Roger P.	Willmar
	Michelson, Henry E.	Minneapolis
	Michienzi, Leonard J.	St. Paul
†	Mickelsen, Emma F.	Minneapolis
	Mickelson, John C.	Mankato
	Midboe, Gilbert T.	Forest Lake
	Middlebrook, John E.	Minneapolis
	Midthune, Andreen S.	Lake Park
†	Mielke, John E.	Rochester
	Miettunen, John B.	Hibbing
	Milhaupt, Emmett N.	St. Cloud
	Miller, Albert G.	St. Paul
†	Miller, Alfred	Rochester
	Miller, H. Dawes	Minneapolis
	Miller, Harold E.	Minneapolis
	Miller, Herman	Austin
	Miller, Hugo E.	Minneapolis
	Miller, J. Carlton	Minneapolis
†	Miller, John W., Jr.	Rochester
	Miller, Roland D.	Rochester
	Miller, Ross H.	Rochester
†	Miller, Victor I.	Belmont, California
	Miller, W. Eugene	Rochester
	Miller, William P.	Minneapolis
	Miller, William T.	St. Paul
	Miller, Winston R.	St. Paul
	Miller, Zondal R.	St. Paul
	Millett, D. Keith	Minneapolis
	Millikan, Clark H.	Rochester
	Mills, John L.	Winnebago
	Mills, Stephen D.	Rochester
	Milnar, Frank J.	St. Paul
	Milroy, Thomas W.	Minneapolis
	Milton, John S.	Minneapolis
	Minder, John G.	Mound
	Minge, Raymond K.	Worthington
	Minsky, Armen A.	Minneapolis
	Mishek, Charles J.	St. Paul
	Mitby, Irvin L.	Minneapolis
	Mitchell, Berton D.	Minneapolis
	Mitchell, Edward C.	Mound
	Mitchell, George S.	St. Paul
	Mitchell, Mancel T.	Minneapolis
	Mixer, Harry W.	Minneapolis
	Mlinar, Joseph P.	Austin
	Moberg, Clarence W.	Detroit Lakes
	Mock, Charles J.	Virginia
	Moe, John H.	Minneapolis
	Moe, Thomas	Moose Lake
	Moe, W. Wyatt	Minneapolis
	Moehn, John T.	Minneapolis
†	Moeller, Henry G., IV.	Rochester
	Moen, Johannes K.	Minneapolis
†	Moersch, Frederick P.	Rochester
	Moertel, Charles G.	Rochester
	Molander, Herbert A.	St. Paul
	Molenaar, Robert E.	Cannon Falls
	Moller, Jurgen	Farmington
	Mollers, Theodore P.	Fort Snelling
	Molnar, George D.	Rochester
	Monahan, Robert H.	St. Paul
	Monge, James J.	Duluth
	Monserud, Nels O.	Cloquet
	Monson, Einer M.	Minneapolis
	Monson, Leonard J.	Canby
†	Montgomery, Hamilton	Rochester
	Mooney, Robert D.	St. Paul
†	Moore, Gordon L., II	Rochester
	Moore, Irvin H.	Hopkins
	Moorhead, Marie	Minneapolis
	Moos, Daniel J.	Minneapolis
†	Moquin, Marie A.	St. Paul

	Moral, Harvey M.	Minneapolis
	Moran, Leo J.	New Brighton
†	Morehead, Dewey E.	Bodega Bay, California
†	Moren, J. Adelaide	White Bear Lake
	Morgan, Hugh O.	Amboy
	Mori, Hideo	Grand Meadow
	Moriarty, James A.	Minneapolis
	Moriarty, Joseph D.	Coon Rapids
	Moriarty, M. Berenice	St. Paul
	Mork, A. Harold	Anoka
	Mork, Frank E.	Anoka
	Mork, Frank E., Jr.	Minneapolis
	Morlock, Carl G.	Rochester
	Morrison, Charlotte J.	Minneapolis
	Morrow, George W., Jr.	Rochester
†	Morse, Morton P.	LeRoy
†	Morse, Robert M.	Rochester
	Morse, Roger D.	LeRoy
†	Morsman, L. William	Hibbing
†	Mortensen, Nels G.	Minneapolis
	Mortenson, Howard O.	Menahaga
	Mosby, Maurice E.	Long Prairie
	Mosser, Donn G.	Minneapolis
	Moulton, Keith B.	Decatur, Ill.
	Mouritsen, Glenn J.	Fergus Falls
	Moyer, John B.	Duluth
	Moyer, Leonard B.	Minneapolis
	Moyer, Richard R.	Hibbing
	Muchmore, Harold G.	St. Paul
	Muchow, Gene C.	Austin
	Mueller, LeRoy E.	Hendricks
	Mueller, Rudolph B.	Richmond
	Muesing, Mark A.	Tyler
	Muesing, William J.	New Ulm
	Mulder, Donald W.	Rochester
	Mulholland, William M.	Minneapolis
	Muller, A. Eugene	North St. Paul
	Muller, John J.	Hibbing
	Muller, Sigfrid A.	Rochester
	Mulligan, Arthur M.	Brainerd
	Mullin, Gerald T., Jr.	Minneapolis
	Mulvahill, John E.	Minneapolis
	Mundahl, Harold R.	St. Paul
†	Mundy, Betty Lee	Rochester
	Munger, James E.	Duluth
	Munkittrick, Ronald C.	Minneapolis
	Munneke, Lyle	Clara City
	Munson, Martin S.	Moose Lake
	Murn, Thomas G.	St. Cloud
	Murphy, Edmund P.	Minneapolis
	Murphy, Jack T.	St. Paul
	Murphy, Joseph E.	Marshall
	Murphy, Thomas R.	Stillwater
	Murray, Elisabeth M.	Minneapolis
†	Murray, James J.	Rochester
	Murray, Robert A.	Hibbing
	Murray, Robert A., Jr.	St. Cloud
	Murray, Roger C.	St. Paul
	Murtaugh, Robert J.	Wadena
	Musachio, Nicholas F.	St. Paul
	Muske, Marvin M.	Minneapolis
	Mussey, Mary E.	Rochester
	Musty, Nicholas J.	Minneapolis
	Myers, Jay A.	Minneapolis
	Myers, John W.	Canby
	Myers, Theodore P.	Albert Lea
	Myers, Thomas T.	Rochester
	Myhre, James A.	Minneapolis
	Myre, Clifford R.	Paynesville

N

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	Nagobads, V. George	Minneapolis
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	Nash, Eldore B.	Minneapolis
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	Naslund, Ames W.	Minneapolis
	Nauth, Bernard S.	Minneapolis
	Navratil, Donald R.	Glencoe
	Neal, Joe M.	Minneapolis
	Nealy, Donald E.	Adrian
	Neary, Richard P.	Minneapolis
	Neault, Roger W.	Rochester
	Neel, Harry B.	Albert Lea
	Neff, Walter S.	Virginia
	Neher, Frederick J.	St. Paul
	Neibergs, Lydia I.	St. Paul
	Neibergs, Paul	St. Paul
	Neils, Vernon E.	St. Cloud
	Nelimark, Donald R.	Virginia
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†	Nelson, Bernice A.	Minneapolis
	Nelson, Carleton A.	Minneapolis
	Nelson, C. Barton	Minneapolis
	Nelson, Clayton E. J.	Albert Lea
	Nelson, David J.	Minneapolis
	Nelson, Edward N.	Minneapolis
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	Nelson, George E.	Minneapolis
	Nelson, Gerald E.	Chaska
	Nelson, Glenn E.	Fairfax
	Nelson, Gunard A.	Minneapolis
	Nelson, Harvey	Minneapolis
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†	Nelson, J. Phillip	Rochester
	Nelson, Lloyd	Minneapolis
	Nelson, Loren E.	St. Paul
*†	Nelson, Louis A.	St. Paul
	Nelson, Louis A., Jr.	St. Paul
	Nelson, Luther A.	Rush City
	Nelson, Maxine O.	Minneapolis
	Nelson, Maynard C.	Minneapolis
	Nelson, O. L. N.	Minneapolis
	Nelson, Robert H.	Benson
	Nelson, Roy A.	Fergus Falls
	Nelson, Wallace I.	Minneapolis
	Nerenberg, Sidney	Minneapolis
	Nesheim, Martin O.	Emmons
	Ness, Duane E.	Wadena
	Ness, Richard A.	Fergus Falls
	Nesse, James A.	Austin
	Nesset, Lawren B.	Minneapolis
	Nesset, William D.	Minneapolis
	Nesvacil, Leon	St. Paul
	Neumaier, Arthur	Glencoe
	Neumann, Roland F., Jr.	Minneapolis
	Neumeister, Charles A.	Minneapolis
†	Newcomer, Albert D.	Rochester
	Newton, St. Elmo, III	Seattle, Wash.
	Niazi, Suad A.	Granite Falls
	Nichols, Donald R.	Rochester
	Nichols, Thomas O.	St. Paul

	Nicholson, Richard W.	Fergus Falls
	Nickerson, John R.	Fairmont
	Nickerson, Neil D.	Fairmont
	Nielsen, David J.	Minneapolis
	Nietfield, Aloys B.	Sauk Centre
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	Nimlos, Kenneth O.	St. Paul
†	Nimlos, Lenore O.	St. Paul
	Ninneman, Newton	St. Peter
#	Nirschl, Robert P.	Long Island, New York
	Nisius, George F.	Duluth
	Nisswandt, Albert L.	Duluth
	Nixon, James B.	Crosby
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	Nolan, Robert K.	Minneapolis
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	Nollet, Donald J.	Hibbing
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	Noran, Harold H.	Minneapolis
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	Nord, Robert E.	Minneapolis
†	Nordin, Gustaf T.	Honolulu, Hawaii
†	Nordland, Martin	Minneapolis
	Nordland, Martin A.	Minneapolis
	Nordlund, Mildred E.	McClellan, A.F.B., California
	Nordman, Willard F.	Mora
	Norman, David D.	St. Paul
	Norman, Franklin C.	Minneapolis
	Norman, Mark L., Jr.	Minneapolis
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	Norval, Mildred A.	Minneapolis
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	Nuebel, Charles J.	Long Beach, California
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	Nuessle, William F.	St. Louis Park
	Nuetzman, Arthur W.	Faribault
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	Nydahl, Malvin J.	Minneapolis
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	Nye, Lillian L.	St. Paul
	Nygren, William T.	Braham
	Nywall, Dean D.	Slayton

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	O'Brien, William A.	Minneapolis
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†	O'Donnell, Kevin T.	Rochester
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	O'Kane, Thomas W.	St. Paul
	O'Keefe, James P.	St. Cloud
	O'Leary, John B.	Brainerd
	O'Malley, Valentine	St. Paul
	O'Neill, John C.	Duluth
	O'Neill, Nial C.	St. Paul
	O'Phelan, E. Harvey	Minneapolis
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	O'Rourke, William J.	Austin
†	Oberstein, Barry J.	Rochester
†	Obetz, Samuel W.	Rochester
	Ochsner, Clarence G.	St. Paul
	Ockuly, Orville E.	St. Paul
	Odland, Donald M.	Luverne
	Odland, Mark E.	Detroit Lakes
	Odland, Olin M.	Granite Falls
	Oeljen, Siegfried C.	Waseca
†	Oels, Helen C.	Rochester
	Officer, Charles D.	Burnsville
†	Ogden, Warner	St. Paul
†	Ohage, Justus	St. Paul
	Olafson, Richard A.	Fargo, N. D.
	Olavs, Olga	Minneapolis
	Olds, George H.	New Richland
	Olfelt, Paul C.	Minneapolis
	Olinger, John N.	St. Cloud
	Olive, John T., Jr.	Mankato
	Oliver, Irwin L.	Graceville
	Olmanson, Edmund G.	St. Peter
	Olmanson, M. Donald	St. Peter
	Olmanson, Vern	St. Peter
	Olsen, E. George	Minneapolis
	Olsen, Jay R.	Minneapolis
	Olsen, Ralph L.	St. Paul
*	Olson, Albert E.	Duluth
	Olson, Albert J.	Owatonna
	Olson, Alton C.	Minneapolis
	Olson, Archie O.	Duluth
	Olson, Barbara F.	South St. Paul
	Olson, C. Kent	Minneapolis
	Olson, Carl J.	Minneapolis
	Olson, Detlof M.	Minneapolis
	Olson, Duane C.	Minneapolis
	Olson, Ernest A.	Rochester
	Olson, Frances P.	Fergus Falls
	Olson, Grant E.	West Concord
	Olson, Gregory M.	Litchfield
	Olson, Lillian A.	Bemidji
†	Olson, Olaf A.	Minneapolis
	Olson, Philip A.	Minneapolis
	Olson, Richard E.	Chaska
	Olson, Rolland A.	Wayzata
	Olson, Robert T.	Canby
	Olson, Robert W.	Minneapolis
	Ongley, Patrick A.	Rochester
#	Onofrio, Burton M.	Chevy Chase, Md.
	Onsgard, L. Kenneth	Houston
†	Onstad, Gerald R.	Rochester
	Opheim, Richard H.	Minneapolis
	Opitz, Joachim L.	Rochester
	Oppegaard, Chester L.	Crookston
	Oppen, E. Gerhard	Minneapolis
	Oppen, Melvin G.	Wayzata
	Opsahl, Lawrence	Willmar
	Opstad, Earl T.	Minneapolis
	Orandi, Mehdi	Fergus Falls
	Orbuch, Martin W.	Minneapolis
	Orkin, Milton	Minneapolis
	Orn, Duane L.	Minneapolis
	Orr, Burton A.	Faribault
	Osborn, Donald O.	Austin
†	Osekowsky, Henry J.	Minneapolis
	Osmundson, Philip J.	Rochester
	Ostergaard, Erling	Elbow Lake
†	Ostergren, Edward W.	St. Paul
	Ott, Eugene C.	Minneapolis
*†	Otto, Henry C.	Frazee
	Ouellette, Alfred J.	St. Paul
	Ourada, Anthony L.	Fairmont

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	Overland, Arnold J.	Greenbush
	Owen, Charles A., Jr.	Rochester
	Owen, Richard R.	Minneapolis
	Owens, Ben P.	Hibbing
	Owens, Frederick M., Jr.	St. Paul
	Owens, William A.	Montevideo

P

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	Paciotti, Vincent J.	Hibbing
†	Packovich, Milan J.	Rochester
	Page, Raymond L.	Minneapolis
	Paisner, Hyman M.	Minneapolis
	Palen, Benjamin J.	Minneapolis
	Palm, Neil M.	St. Paul
	Palmer, Clinton F.	Albert Lea
	Palmer, Harry A.	Blackduck
	Palumbo, Pasquale J.	Rochester
	Papermaster, Ralph	Minneapolis
	Papermaster, Theodore C.	Minneapolis
†	Pappas, George	Rochester
	Paris, Jaime	Rochester
	Park, Wilford E.	Minneapolis
	Parker, Charles W.	Wadena
†	Parker, Joseph C., Jr.	Rochester
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	Parker, Robert L.	Rochester
	Parker, Warren E.	Sebeka
	Parker, Wilbert H.	Chisholm
	Parkhill, Edith M.	Rochester
	Parkin, Thomas W.	Rochester
	Parrott, John C.	Minneapolis
	Parson, E. Irvine	Duluth
	Parson, E. Lillian B.	Elbow Lake
†	Parson, Lester R.	Elbow Lake
	Parsons, R. A.	St. James
	Parsons, Ralph L.	Trimont
†	Parsons, William R.	Rochester
	Pasek, Antone W.	Cloquet
	Patch, Orien B.	Duluth
	Pattee, James J.	Minneapolis
	Patten, John C.	Austin
	Patterson, Hugh D.	Slayton
†	Patterson, William L.	Fergus Falls
	Paule, William J.	Minneapolis
	Paulson, Elmer C.	St. Paul
	Paulson, John A.	Rochester
	Paulson, Wallace J.	St. Paul
	Pawlyszn, Julian	Fergus Falls
	Payne, Richard E.	Virginia
†	Payne, Stanley R.	Rochester
	Payne, W. Spencer	Rochester
†	Peacock, William F., III	Rochester
	Pearson, Bror F.	Shakopee
†	Pearson, Fritz R.	St. Paul
†	Pearson, John E.	Rochester
	Pearson, Malcolm M.	St. Paul
	Pease, Gertrude L.	Rochester
†	Peck, Donald A.	Pittsburgh, Pa.
†	Pedace, Francis J.	Rochester
	Pedersen, Arthur H.	St. Paul
	Pedersen, Robert L.	Brainerd
	Pedersen, Roy C.	Duluth
	Peikert, Carl F.	Forest Lake
	Peluso, Charles R.	Minneapolis
	Pelzl, Charles R.	Pine River
†	Pemberton, John deJ.	Rochester
	Penk, Engward L.	Springfield
	Penn, George E.	Mankato
	Peper, Martin C.	Minneapolis
†	Pequegnat, Edouarde P.	Rochester
	Perkins, Douglass E.	Alexandria
	Perlman, Everett C.	Minneapolis
	Perlman, Herschel L.	Minneapolis
	Perpich, Irene Kosiak	Virginia
	Perry, Harold O.	Rochester
#	Perry, Hugh, Jr.	A.P.O. New York, New York
	Perry, John F., Jr.	St. Paul
	Person, Duane F.	Britt
†	Pertl, Albert L.	Canby
	Peteler, Jennings C. J.	Minneapolis
	Peters, Gustavus A.	Rochester
	Petersen, Bryon D.	Minneapolis
	Petersen, Deane A.	Wayzata
	Petersen, Donald H.	Willmar
	Petersen, Glenn L.	Minneapolis
	Petersen, Robert T.	St. Cloud
	Petersen, William E.	Minneapolis
	Peterson, Alan A.	Rochester
	Peterson, Alvin C.	Mora
	Peterson, David B.	St. Paul
	Peterson, Donald H.	St. Paul
	Peterson, Edward A.	St. Paul
	Peterson, Edward N.	Virginia
†	Peterson, Hamlet A.	Rochester
	Peterson, Harold O.	Minneapolis
	Peterson, Herbert W.	Rochester
	Peterson, Joel L. E.	St. Paul
	Peterson, John A.	Minneapolis
	Peterson, John H.	Duluth
	Peterson, John O.	Hastings
	Peterson, John R.	Rushford
	Peterson, Kenneth A.	Marshall
	Peterson, Kenneth H.	Hutchinson
	Peterson, Lowell F. A.	Rochester
	Peterson, Oliver H., Jr.	Minneapolis
	Peterson, Palmer A.	Cashton, Wisconsin
#	Peterson, Richard A.	Seattle, Washington
	Peterson, Roy A.	Vesta
	Peterson, Roy L.	White Bear Lake
	Peterson, Stanley C.	Austin
	Peterson, Theodore A.	Minneapolis
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	Peterson, Willard C., Jr.	Minneapolis
	Peterson, Willard E.	Willmar
	Peterson, Willard H.	Minneapolis
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†	Petit, Leon J.	Minneapolis
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	Petroske, James L.	Hastings
	Pettersen, George R.	Aitkin
	Pewters, John T.	Minneapolis
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	Phares, Otto C.	St. Cloud
†	Phelps, Kenneth A.	St. Petersburg, Florida
	Phelps, Robert D.	Minneapolis
	Phibbs, Clifford M.	Minneapolis
	Phillips, Leonard	St. Paul
	Philp, David R.	Watertown
	Pierce, Robert B.	Mountain Lake
	Pierson, Roy F.	Slayton

Pilling, Loran F.	Rochester
Pincus, Mitchell	Minneapolis
Pinell, Octavio (Midence)	Rochester
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Pistulka, Rolland D.	Chaska
Plasha, Matthew K.	Coon Rapids
Plass, Herbert F. R.	Minneapolis
Pleissner, Karl W.	Minneapolis
Plimpton, Nathan C.	Minneapolis
Plotke, Harry L.	St. Paul
Plucker, Milton W.	Worthington
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Pohl, John F.	Minneapolis
† Poirier, Joseph A.	Forest Lake
Pollak, Kurt	Minneapolis
Pollard, William S.	Duluth
Polley, Howard F.	Rochester
Pollman, Stanley E.	Thief River Falls
Pollock, Anthony J.	Minneapolis
Polski, Paul G.	South St. Paul
Polzak, Jacob A.	Minneapolis
Pone, John J.	Minneapolis
Ponterio, James E.	Shakopee
Pool, T. Lloyd	Rochester
Popadiuk, Peter	Minneapolis
Popoff, Russel G.	Graceville
Popovich, Dragojla	Milwaukee, Wisconsin
Popowich, John G.	Minneapolis
† Poppe, Frederick H.	Coral Gables, Florida
Poppie, Robert W.	Brainerd
† Porter, Oliver M.	Minneapolis
Post, Edmund A.	St. Paul

† Potter, Myron T., II	Rochester
Potter, Robert B.	Minneapolis
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Power, John E., Jr.	Duluth
† Powers, Donald W.	Rochester
Powers, Robert L.	St. Paul
† Pratt, Fred J.	Minneapolis
Pratt, Fred J., Jr.	Minneapolis
Pratt, Joseph H., Jr.	Rochester
Prentice, Walter B.	St. Paul
Prem, Konald A.	Minneapolis
Prespare, Charles	Waconia
Preston, Frank S., Jr.	Minneapolis
Price, William E.	Minneapolis
Prickman, William E.	Minneapolis
Priest, Robert E.	Minneapolis
Priestley, James T.	Rochester
† Prim, Joseph A.	Minneapolis
Prlina, Isaac M.	Virginia
Proeschel, Ray K.	Willmar
Proffitt, William E.	Minneapolis
Proshek, Lumir C.	Minneapolis
Proud, Harry S.	St. Paul
Pugh, David G.	Rochester
Pulec, Jack Lee	Rochester
Pumala, Erven E.	Warren
Purnell, Don C.	Rochester
Purves, G. Harland	Buffalo
Puumala, Barbara M.	Cloquet
Puumala, Reino H.	Cloquet
Puumala, Ricard R.	Cloquet

Q

† Quattlebaum, Frank W.	St. Paul
Quello, Robert O. B.	Minneapolis
Quiggle, Arthur B.	Minneapolis
Quist, Henry W., Jr.	Minneapolis

R

Raab, David E.	Minneapolis
Raaen, Olaf J.	St. Paul
Rabcevich, Anatole	St. Paul
Racer, Harley J.	Minneapolis
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Raetz, Sylvester J.	Maple Lake
Raile, Richard B.	Minneapolis
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Ralph, James R.	St. Paul
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Ramlow, Ralph M.	St. Paul
† Ramsey, Walter R.	St. Paul
Randall, David A.	Minneapolis
† Randall, Lawrence M.	Rochester
Randall, Raymond V.	Rochester
Ransom, H. Robert	Osseo
Raphael, Hugh A.	Rochester
Rasmussen, Ramby C.	St. Paul
Ratelle, Alexander E.	Minneapolis
Raths, Otto N., Jr.	St. Paul
Ravits, Harold G.	St. Paul
† Rawls, William E.	Houston, Texas
Rayner, Ralph R.	Red Wing
Rea, Charles E.	St. Paul
Reardon, Andrew E.	Duluth
Recht, Thomas M.	Minneapolis
Redleaf, Paul D.	St. Paul

Reeber, Erick	Bagley
Reed, Henry H.	Duluth
† Reed, John H., Jr.	Rochester
Reed, Paul	Virginia
Reed, Ralph R.	Rochester
Reed, Sheldon C.	Minneapolis
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Regan, John J.	Minneapolis
Regnier, Edward A.	Minneapolis
Reichel, Samuel M.	Minneapolis
Reichelderfer, Charles F.	Staples
Reichelt, Leland G.	Wadena
Reid, James W.	South St. Paul
Reif, Harold A.	Minneapolis
Reif, Henry J.	St. Cloud
Reif, Robert W.	White Bear Lake
Reiher, Jean	Rochester
Reiley, Richard E.	Minneapolis
Reinhardt, James H.	Alexandria
Reiser, Milton P.	Minneapolis
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ReMine, William H., Jr.	Rochester
Remole, William D.	Minneapolis
Remsberg, Robert R.	Tracy
† Replogle, William H.	Los Angeles, California
Resch, Joseph A.	Minneapolis

	Restall, Charles J.	Rochester
	Reynolds, Donald P.	Minneapolis
	Rheault, J. Gerald	Rochester
†	Rhodes, Rollie E.	Rochester
	Rholl, Arnold O.	Minneapolis
	Rice, Carl O.	Minneapolis
	Rice, Fred A.	Minneapolis
	Rice, Hagbart G.	Moorhead
	Rice, William H.	St. Cloud
	Richards, Albert M.	St. Paul
	Richards, William B.	St. Cloud
	Richardson, Edward J., Jr.	St. Paul
	Richardson, Robert J.	Minneapolis
†	Richdorf, Lawrence F.	Minneapolis
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	Richter, David J.	Virginia
	Rick, Paul F. W.	St. Paul
	Rieke, Wellington W.	Wayzata
	Rieschl, Elizabeth K.	Jordan
	Riggs, Byron L., Jr.	Rochester
	Riley, Fenwick C.	Rochester
	Rimas, Matthew J.	Comfrey
	Ringhofer, Lawrence	New Ulm
	Ringle, Otto F.	Walker
	Rinkey, Eugene	St. Paul
	Riordan, Elsie M.	Minneapolis
	Ripple, Rudolph J.	St. Paul
	Ripple, Rudolph J., Jr.	Minneapolis
	Risch, Ronald E.	Minneapolis
	Risser, Alden F.	Stewartville
	Ritchie, Wallace P.	St. Paul
	Ritt, Albert E.	St. Paul
	Ritter, Donald G.	Rochester
	Rizer, Dean K.	Minneapolis
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	Roach, Donald E.	St. Paul
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	Roberts, Lewis J.	Minneapolis
	Roberts, Oliver W.	Owatonna
	Roberts, Stanley W.	Minneapolis
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†	Robertson, Paul A.	Austin
	Robinson, Cortland O.	Minneapolis
	Robinson, William W.	New London
	Rock, William H.	Anoka
	Rocknem, Robert E.	Minneapolis
	Rockwell, Curtiss V.	Minneapolis
	Rockwood, Philo H.	Fergus Falls
	Rodgers, Richard S.	Minneapolis
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	Roemer, Henry J.	Winona
	Rogers, Charles W.	Winona
	Rogin, Norton	Minneapolis
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	Roholt, Hartvig B.	Bemidji
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	Rollie, Orris O.	St. Paul
	Rollins, Pat	Minnetonka
	Rome, Howard P.	Rochester
	Romness, Kenneth B.	Mound
	Rondeau, Eugene T.	Two Harbors
	Rooke, Edward D.	Rochester
	Rorem, Joseph A.	Appleton
	Rosenbaum, David L.	Minneapolis
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	Rosenfield, Abraham B.	Minneapolis
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	Rosenow, John H.	Minneapolis
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	Rosenthal, Robert	St. Paul
†	Rosenwald, Reuben M.	Robbinsdale
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	Rossberg, Raymond A.	Morris
	Rossen, Ralph	Minneapolis
	Rossing, Robert G.	San Antonio, Texas
	Rotenberg, Robert J.	Minneapolis
	Rotenberg, Samuel	Huntington Park, Calif.
	Roth, Albert H.	Deer River
	Roth, Frederick D.	Mankato
	Roth, George C.	St. Paul
	Roth, Sanford H.	Rochester
	Rothnem, Morris S.	Minneapolis
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	Roust, Henry A.	Montevideo
	Rovelstad, Randolph A.	Rochester
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	Rowe, Richard G.	Silver Bay
	Rowles, Everett K.	Coleraine
	Roy, Phil C.	St. Paul
	Rozycki, Anthony T.	St. Cloud
	Rubin, Jacob S.	Crookston
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	Rucker, William H.	Minneapolis
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	Rudie, Peter S.	Duluth
	Rudie, William D.	Duluth
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	Rukavina, John G.	St. Paul
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	Runquist, Richard K.	Cambridge
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†	Rutledge, Lloyd H.	Detroit Lakes
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	Ryan, Joseph M.	St. Paul
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	Ryding, Vincent	Ames, Iowa
	Rydland, Arne D.	Minneapolis
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	Rynda, Edwin	New Prague
	Rynearson, Edward H.	Rochester
	Rynearson, Robert R.	Rochester
	Rysgaard, George N.	Northfield

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	Salovich, Elmer R.	Minneapolis
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	Sandeen, Robert M.	Buffalo
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	Sather, Richard N.	Fosston
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	Sayre, George P.	Rochester
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	Segal, Martin A.	Minneapolis
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	Seifert, Milton H.	Excelsior

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	Sidell, Franklin D.	Minneapolis
	Siegel, Clarence	St. Paul
	Siegel, John S.	Virginia
	Siegmann, William C.	Minneapolis
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	Sigel, Melvin E.	Minneapolis
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	Silas, Ralph M.	Minneapolis
	Silver, John D.	Minneapolis
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	Silverstein, Murray N.	Rochester
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	Simons, Leander T.	St. Paul

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	Simonton, Kinsey M.	Rochester
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	Sinamark, Andrew	Hibbing
	Singer, Benjamin J.	St. Paul
	Sinning, John E., Jr.	Minneapolis
	Sinykin, Melvin B.	Minneapolis
	Sipe, James W.	Coon Rapids
*	Siperstein, David M.	Minneapolis
	Sisk, Harvey E.	St. Cloud
	Sisler, Clifford E.	Grand Rapids
	Sjoding, J. Donald	Mankato
	Sjostrom, Lawrence E.	St. Peter
	Skaife, William F.	Benson
	Skaug, Harold M.	Chatfield
	Skinner, Abbott	St. Paul
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	Skjold, Arthur C.	Minneapolis
	Skogerboe, Rudolph B.	Karlstad
	Slack, William J.	Duluth
	Slocumb, Charles H.	Rochester
	Smiley, Donald P.	St. Paul
	Smiley, John T.	Minneapolis
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	Smisek, Frank M.	Minneapolis
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	Smith, George R.	Hutchinson
†	Smith, George R.	Rochester
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	Smith, Harry J.	Lake Crystal
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	Smith, Lloyd A.	Willmar
	Smith, Lucian A.	Rochester
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†	Smith, Myron W.	Red Wing
	Smith, Nadine G.	Minneapolis
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	Smith, Paul M.	Lake Crystal
	Smith, Ralph E.	Rochester
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	Smith, Richard D.	Rochester
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	Sommerdorf, Vernon L.	St. Paul
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	Sones, Donald A.	Rochester
	Sonnesyn, Nels N.	Le Sueur
	Sontag, David W.	Lake City
	Sorem, Milton B.	St. Paul
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	Spang, William M.	Duluth
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	Spiekerman, Ralph E.	Rochester
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	Spink, Wesley W.	Minneapolis
	Spittell, John A., Jr.	Rochester
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	Sponsel, Kenath H.	Minneapolis
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	Stratte, Jon R.	Stillwater
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	Strem, Edward L.	St. Paul
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	Strickler, Jacob H.	Minneapolis
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	Stroebel, Charles F., Jr.	Rochester
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	Swendseen, Carl J.	Minneapolis
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†	Thompson, Gershom J., Jr.	Rochester
	Thompson, James P., Jr.	Rochester
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